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TWO CASES OF SYRINGOMYELIA AND SYRINGOBULBIA, OBSERVED CLINICALLY OVER MANY YEARS, AND EXAMINED PATHOLOGICALLY.

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SYRINGOMYELIA, although perhaps not so unusual as at one time it was supposed to be, is a very interesting disease, because of the clear association which it is possible to trace between the anatomical change in the spinal cord and bulb, and the clinical condition. The two cases which we are about to relate are perhaps unusual because of the long periods during which it was possible to observe them carefully. They also have a special interest because of the striking manner in which the clinical course differed in the two cases. In the first patient the condition underwent no change of consequence during the long period of twenty-four years in which one of us (J. T.) had him under almost continuous observation; in the second, who was also under observation for a long period, viz., nineteen years, there was on the contrary a slow but steady deterioration in the physical condition determined by the gradual spread of muscular weakness and sensory change, the result no doubt of corresponding changes in the condition of the spinal cord. The detailed description of the morbid changes in the spinal cords, for which two of us (J. G. G. and J. P. M.) are responsible, explains to some extent this difference.

H. M., a pastrycook by occupation, was admitted to the National Hospital, Queen Square, under Dr. Hughlings Jackson on May 15, 1893. He was at this time 23 years of age and had previously been under Dr. Jackson's care at the London Hospital. He said that four and a half years before admission he had experienced pain in the right occipital region, with numbness in the arms. Three months later there developed squinting of the right eye and diplopia, and a few days later there was numbness of the right side of the face and complete loss of sensation here which lasted for a fortnight. This, he said, had since practically cleared up. Four days after experiencing numbness of the face he noticed that the right side of the face was motionless, and he stated his articulation was indistinct and the tongue on protrusion went to the right. For the last four months before admission the occipital pain had been worse, and there was tingling and loss of feeling down the right arm and leg.

FIG. 1.—Case I. Patient in 1893.

FIG. 2.—Case I. Patient in 1915.

There was nothing of significance in his family history or in his personal history. He had had no serious illness and he denied venereal disease.

On admission he was found to have a marked right internal strabismus due to complete paralysis of the right sixth nerve. There was also complete facial paralysis on the same side and the tongue protruded to the right. The right side of the tongue was much wasted, and although the temporal and masseter muscles on both sides were strong and active, the jaw dropped to the left when the mouth was widely opened. There was a good deal of wasting about the shoulders, more marked on the right side, and although the trapezius and other

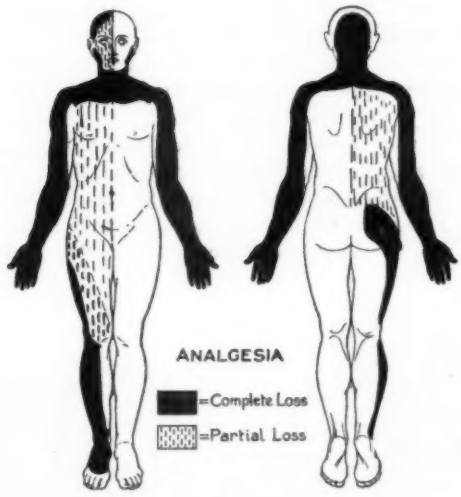


FIG. 3A.—Case I. Analgesia in 1893.

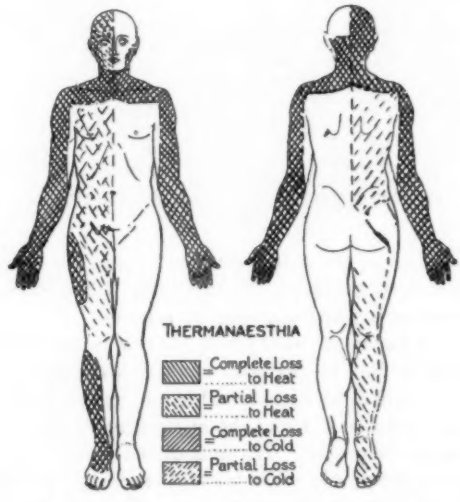


FIG. 3B.—Case I. Thermanæsthesia in 1893.

muscles of the shoulder-girdle all responded to a faradic current on this side, a stronger current had to be used than was sufficient to produce a good contraction on the other side. There was no wasting of the lower limbs; the knee jerks were present and there was no ankle clonus.

The sensory changes were very distinct and interesting. They are so graphically represented in the accompanying diagrams that no further description seems called for. (Figs. 3A, B and C.)

The diagnosis in this case was not difficult, and although at that time—1893—we were not very familiar with syringomyelia, there was no hesitation in concluding that this was a case of that nature. It was apparent that the morbid process had affected not only the spinal cord, especially in its cervical portion, but had also spread upwards so as to involve bulbar and pontine

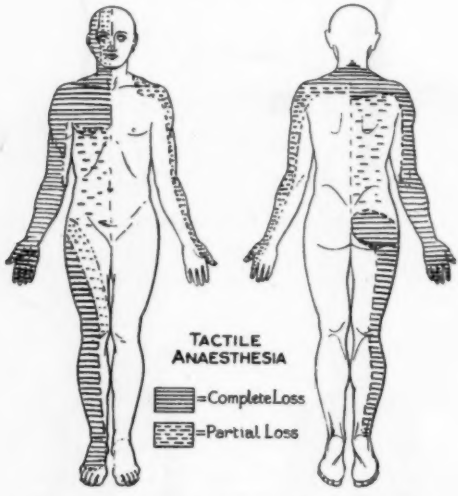


FIG. 3C.—Case I. Tactile anæsthesia in 1893.

structures, as was shown in the wasting of the tongue, the facial paralysis, and the paralysis of the sixth nerve on the right side. The sensory changes also indicated involvement of the fifth nerve or its nucleus.

The patient during the next twenty-four years was seen from time to time and examined carefully, but no material change developed. He enjoyed fair health, although he complained a good deal from time to time of pains in his head and limbs. He married but had the misfortune to lose his wife in 1916 and became very much depressed. He committed suicide by hanging in the following year, having previously asked his brother-in-law to communicate with one of us (J. T.) if anything happened to him. Through the kindness of the Coroner a post-mortem examination was allowed, but as this was not carried

out until forty-eight hours after death the sections of the cord were not as good as they might have been had it been possible to make the examination earlier. It will be seen that the examination confirmed the diagnosis.

Case I.—Pathological Examination.

The brain and cord were fixed directly in Müller's fluid, where they remained for over a year. In consequence of this, permanent flexures had taken place at some segments of the cord and the tissue was rather brittle, so that it was impossible to avoid some distortion of the sections. The chief characteristics of the cord at each level could, however, be made out fairly well.

Right. Left.

Fig. 4A.—Medulla near the lower end of the fourth ventricle. *f.*, Mesial fillet; *L.*, lateral extension of the cavity.

The process of gliosis and cavitation extended from the lower half of the medulla to the lower half of the dorsal region of the cord. For the most part the cavity occupied only a small area of the centre of the cord, but was surrounded by a relatively wide zone of gliosis, in which myelinated fibres were absent.

No abnormality was found at a higher level than the upper part of the pons, but the iter of Sylvius was T-shaped, with a ventral and two lateral prolongations. The ventral one extended between the oculo-motor nuclei, but did

not reach as far as the posterior (median) longitudinal bundle. The lateral extensions almost reached the mesencephalic roots of the trigeminal nerves; they were curved slightly forwards, and their walls, which were everywhere covered with ependyma, were crenated and irregular, the ventral wall showing several small bays and creeks.

Beyond this nothing abnormal was found in the pons and mid-brain, except degeneration of ascending tracts, such as the mesial fillet on the left side, which had been interrupted by the morbid process lower down.

The highest section which showed any evidence of abnormal gliosis was one near the lower end of the calamus scriptorius, passing through the middle of the olivary body (fig. 4A). Here the fourth ventricle had a somewhat irregular contour, extending forward as a narrow slit between the hypoglossal nuclei as far as the dorsal margin of the posterior (median) longitudinal bundles. It also sent a shallower extension in on the right side between the hypoglossal nucleus and the dorsal nucleus of the vagus. Both these slits were lined with the normal ependyma of the ventricle. That in the middle line caused no distortion of fibres, but curving round the gliosis which covered the lateral slit a leash of myelinated fibres could be seen to which there was nothing corresponding on the left side.

At this level and extending downwards through the medulla for a short distance, there was a gross atrophy of the cells in the ventral portion of the right inferior olive, and, associated with this, a loss of the olivo-cerebellar fibres arising in them. An examination of sections at the highest level at which this lesion existed disclosed a small Y-shaped cavity. Its longest limb lay between the pyramidal tract and the olive; one of the shorter limbs passed ventralwards and mesialwards through the pyramidal tract, and the other dorsalwards between the olive and the mesial fillet (fig. 4B). From the walls of this cavity gliosis extended into the neighbouring tissues, chiefly along the hilus of the olive for about two-thirds of its extent, but also as continuations of the limbs of the cavity. In the more caudal sections through the olive no cavity could be seen, but the presence of gliosis was shown by the increase in the number and size of the glial cells, and to it the atrophy of the ventral part of the right olive appeared to be due. The lateral part of the pyramidal tract was smaller on the right side than on the left; the shrinkage of this tract was also probably due to its involvement in the gliosis.

Unfortunately serial sections were not made through the upper part of the medulla and the lower part of the pons, part of the tissue having become unusable owing to its long stay in Müller's fluid during the war, so that it was impossible to trace the extent of this cavity; but if either the cavity itself or a band of gliosis spreading out from it, had passed upwards for a short distance in the same relative position it would have interrupted the emerging fibres of the sixth nerve.

The most obvious loss of fibre tracts was in the mesial fillet on the left side, that is, in the more normal half of the medulla. This fillet had almost completely disappeared, and the place normally occupied by it had shrunken so that

the inner border of the olivary nucleus came much nearer to the median raphe than on the right side. There was also considerable atrophy of the rubro-spinal tract on the right side—in fact, no bundle of fibres corresponding to it could

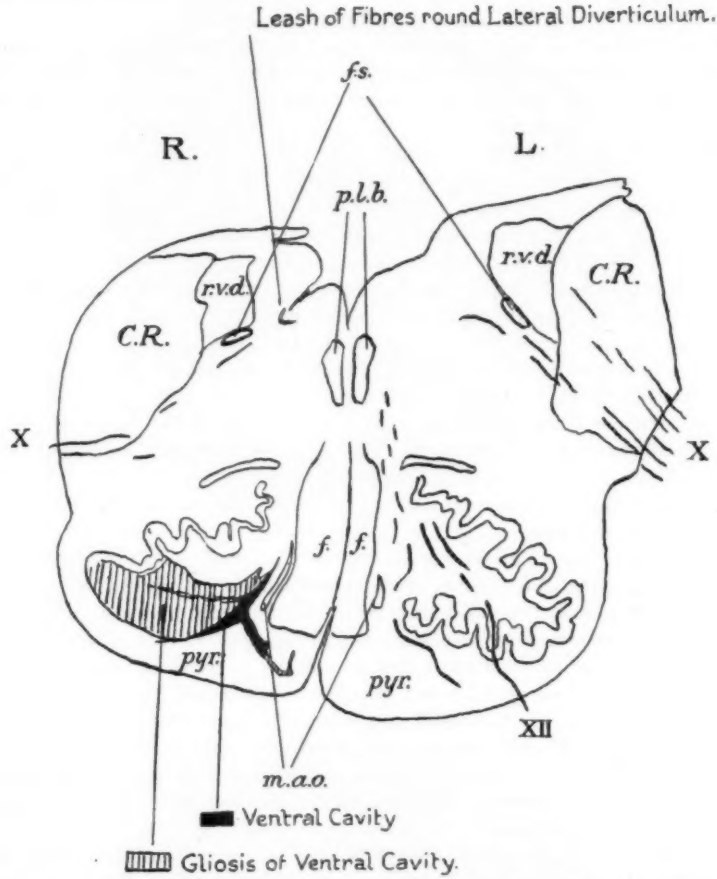


FIG. 4B.—*C.R.*, Corpus restiforme; *f.*, mesial fillet; *m.a.o.*, median accessory olive; *f.s.*, fasciculus solitarius; *p.l.b.*, posterior longitudinal bundle; *pyr.*, pyramid; *r.v.d.*, radix vestibularis descendens.

be definitely made out. The descending root of the trigeminal nerve and the fasciculus solitarius were well represented on both sides, but on the right they were definitely smaller and paler than on the left. The descending root of the right vestibular nerve was represented by far fewer fibres than on the

opposite side, and it and the right fasciculus solitarius had come to lie much nearer to the middle line than the corresponding tracts on the left side. In fact, the whole of the right dorso-lateral part of the medulla at this level had shrunk considerably. It appeared probable that the atrophy of these various fibre tracts was due to a retrograde degeneration of the fibres towards their cells of origin, owing to a lesion at a slightly lower level.

Some internal arcuate fibres were present on the right side at this level, but they were scantier than on the opposite side and more laterally placed. They were intermingled with fibres passing from the opposite olivary nucleus towards the restiform body.

At a level of the medulla corresponding to the tip of the calamus scriptorius (fig. 5) the morbid process was evident as a line of gliosis which passed outwards on the right side through the dorsal part of the hypoglossal nucleus and through the substantia gelatinosa Rolandi (descending or spinal trigeminal nucleus) to about 2 mm. from the lateral surface of the medulla. This band of gliosis ran along the line of the large vessels, which pass dorso-mesially into the medulla between the olivary nucleus and the restiform body. At no level examined in this region was there any gross cavitation, but merely a broad line of gliosis which had interrupted the fibres and caused shrinkage of the parts through which it passed. Here also there was an extension of the cavity of the ventricle forwards between the two hypoglossal nuclei as far as the dorsal part of the posterior (median) longitudinal bundle, but no lateral extension, such as was seen at a rather higher level, could be made out. This mesial extension of the ventricular cavity had caused no obvious destruction of nerve cells or tracts.

The lateral line of gliosis had destroyed the dorsal part of the hypoglossal nucleus, the dorsal longitudinal bundle of Schütz, the major part of the fasciculus solitarius, the substantia gelatinosa Rolandi, and the rubro-spinal tract. It also appeared to have destroyed the descending root of the vestibular nerve on that side, as no fibres corresponding to it could be identified. The region of the nucleus gracilis was greatly shrunken and no fibres could be seen passing from it. Nor could any internal arcuate fibres be seen on that side, except a few laterally placed fibres which obviously arose from the olivary nucleus of the opposite side. As a consequence of this the mesial fillet on the left side was absent and the area it should have filled was shrunken to about half its normal breadth (fig. 5).

In spite of the atrophy of the fillet the posterior (median) longitudinal bundles lay opposite one another, in contra-distinction to what was seen in Case II (fig. 16). The pyramidal tracts, although rather paler than normal, did not show the gross atrophy seen in that case.

The ventral part of the right olivary nucleus was also degenerated here. This appeared to be due to an extension caudalwards of the gliosis surrounding the cavity which was seen at a higher level.

The cells of the right hypoglossal nucleus were atrophied and no root fibres could be seen passing from it. It seems probable that these fibres had been

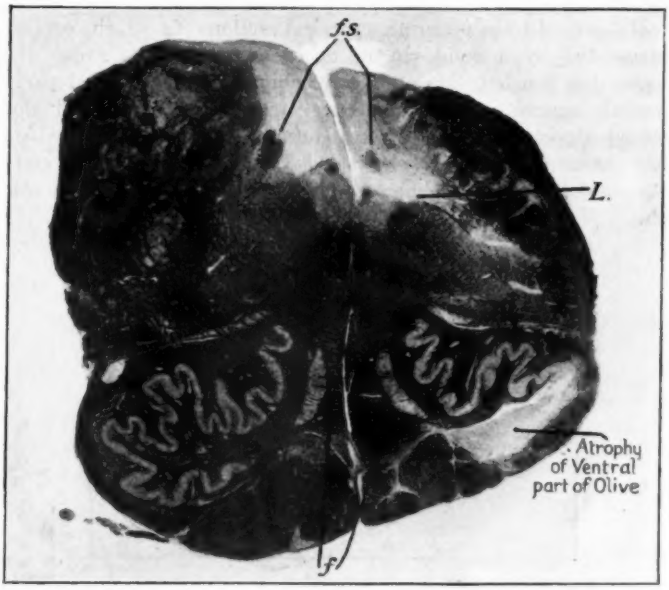


FIG. 5.—Medulla at the level of the tip of the calamus scriptorius. *f.s.*, Fasciculi solitarii; *f.*, mesial fillets; *L.*, lateral gliosis.

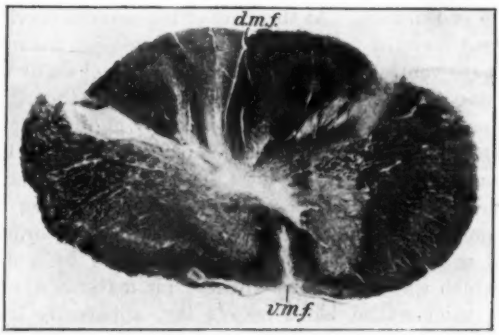


FIG. 6.—Cord at first cervical segment. *d.m.f.*, Dorsal median fissure *v.m.f.*, ventral median fissure.

interrupted by the gliosis and cavitation which lay between the fillet and the olive, and that their cells of origin had consequently undergone a retrograde degeneration.

Spinal Cord.—In the uppermost cervical sections (fig. 6), the central canal was represented by a solid cluster of ependymal cells. Areas of gliosis were present on the left side of it and behind it in the ventral part of the dorso-median septum. From the latter area a cavity extended along the dorso-mesial aspect of the right dorsal horn, the nerve cells in which were much less numerous than on the left side. From the ventro-mesial end of this cavity an area of gliosis ran a short way into the ventral part of the column of Burdach.

FIG. 7.—Third cervical segment of cord. *v.H.*, ventral horns.

At a rather lower level (fig. 7), the cavitation had extended through both dorsal horns and the grey commissure, occupying the situation of the central canal, of which no trace could be seen. At this level the walls of the cavity were lined with a definite layer of gliosis, which varied in thickness and, as in the higher sections, spread into the ventral parts of the column of Goll and the right column of Burdach. At the level of the seventh cervical segment the cavity had spread forward to reach the ventral median fissure, and laterally to the bases of both ventral horns. Extensions ran backwards a short distance down the left dorsal horn, and down the outside of the right dorsal horn almost to the margin of the cord. The wedges of gliosis which were seen at higher levels extending between the columns of Goll and into the right column of Burdach were still evident at this level, the lateral wedge being rather larger than it was above. Except for these wedges, the glial lining surrounded the cavity fairly regularly, and had a sharply marked outer border. The cavity itself was lined over a considerable part of its walls by a definite layer of fibrous tissue, which was continuous with the pia mater of the ventral median fissure. Many thick-walled blood-vessels lay, apparently free, within the cavity; the lumen of some of these was completely occluded, but in others red blood corpuscles could be seen.

The gliosis round the central cavity was, however, still more regular at the level of C 8 (fig. 8). Here it assumed a modified trefoil appearance and corresponded closely to the shape and extent of the central canal of the lumbar cord in Case II (fig. 22). It extended from the ventral median fissure laterally to the bases of both ventral horns, and dorsally a short distance down the dorsal median septum; the lateral areas of gliosis were club-shaped, and their outer ends swollen and rounded. Its outer border, that is the line at which myelinated fibres appeared, was everywhere clear cut and regular.

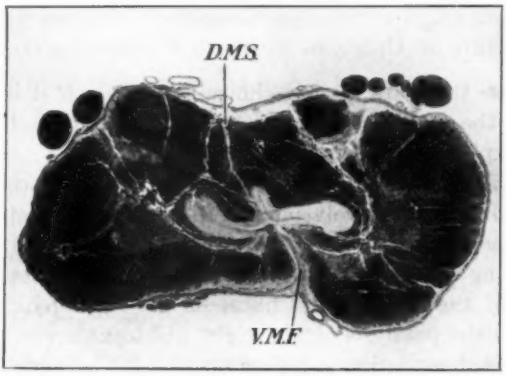


FIG. 8.—Cord at 8th cervical segment. *D.M.S.*, Dorsal median septum; *V.M.F.*, ventral median fissure.

Throughout the cervical region of the cord the nerve roots, both ventral and dorsal, were well myelinated and appeared to be of normal thickness. There was no gross atrophy of tracts apart from the areas of gliosis already described, but the left ventro-lateral column stained rather less deeply than the right.

In the upper thoracic region of the cord the gliosis was limited to an elongated oval running from the neighbourhood of the ventral median fissure through the region of the central canal and dorsally for about two-thirds of the length of the dorsal median septum. In the more caudal segments this area was separated from the ventral median fissure by some myelinated fibres of the white commissure, but its shape and extent remained otherwise constant. Its outer border was as definite and clear cut as in the lowest cervical segments. The cavity, which was limited to a small slit in its centre, showed no lining of connective tissue. The white matter of the cord appeared normal at this region, except for the extreme thinness of the white commissure, and for an area of pallor extending backwards from the dorsal end of the central gliosis along the dorsal median septum. In the lower thoracic region this central gliosis lay definitely behind the column of ependymal cells representing the central canal of the cord, and was separated

from it by a few fine myelinated fibres, some of which ran longitudinally, while others passed across from one side of the cord to the other.

It is impossible from the material at our disposal to determine the level of the lower end of the gliosis in the cord, but it had ceased at the level of the first lumbar segment. From here downwards through the lumbo-sacral enlargement and conus medullaris the central canal was represented by a fairly large rounded clump of ependymal cells, which however did not show the circular arrangement seen in Case II. Their appearance was indeed similar to what is usually found in adult cords at this level.

Relationship of Clinical Signs to Pathological Changes.

In this case there are several clinical signs which it is very difficult to explain by the pathological changes discovered, although others admit of a simple explanation.

The anæsthesia over the area supplied by the right trigeminal nerve was accounted for by the involvement of the substantia gelatinosa Rolandi, and the degeneration in the descending trigeminal root on that side.

The wasting of the right half of the tongue was obviously a result of the atrophy of the nucleus and fibres of the right hypoglossal nerve. Both this and the paralysis of the right abducens nerve were probably due to the area of cavitation and gliosis which lay between the inner end of the right olive and the pyramidal tract. From the material at our disposal we are unable to give an anatomical explanation of the weakness of the muscles supplied by the fifth and seventh nerves on the right side. The nystagmus may be attributed to the lesion of the descending root of the right vestibular nerve.

This case presented the unusual feature that the anæsthesia on the right half of the body was nowhere dissociated. The area of complete loss of appreciation of light touch was exactly the same as that in which pin-prick and heat and cold were not recognized, and where one form of cutaneous sensibility was reduced but not abolished, the others were similiarly diminished. The apparent anomaly admits, however, of a simple explanation. It is generally believed that tactile impressions are conveyed to the thalamus by two sets of fibres; one set crosses in the cord along with the fibres conveying thermal and painful sensations to the opposite ventro-lateral column, while the other ascends in the dorsal columns to the dorsal nuclei of the medulla, and thence by internal arcuate fibres and the mesial fillet. But in this case the fibres passing from the right dorsal nuclei to the left fillet were interrupted by the gliosis which spread out from the floor of the fourth ventricle, and

consequently this path, which in syringomyelia generally remains open for tactile impressions, was broken. No dissociation of cutaneous sensations coming from the right side of the body was therefore possible, since the only effective path for tactile sensibility was the same as that for thermal and painful impressions. The fibres of this path cross in the anterior commissure a considerable distance above their cells of origin in the dorsal horn, and are believed to retain their segmental arrangement until they have crossed. Therefore the fibres arising from cells in the right dorsal horn of the lower lumbar segments may have been interrupted in the lower thoracic region of the cord by a small lateral extension of the central disease, which, however, left intact the fibres arising at lower and higher levels.

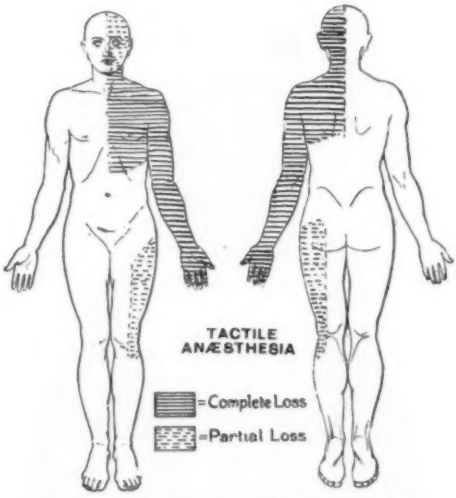


FIG. 9A.—Case II. Anæsthesia in 1902.

The second case which we are about to relate seems to be worthy of record because of the interesting character of the morbid condition from which the patient suffered, and of the long period over which it was possible to observe her and to note the progress of the malady.

She came (A. O.), a girl of 22, to see one of us (J. T.) in the out-patient room at Queen Square, in 1902, complaining of weakness in her left arm and hand which had been present for two or three years. This, she said, had com-

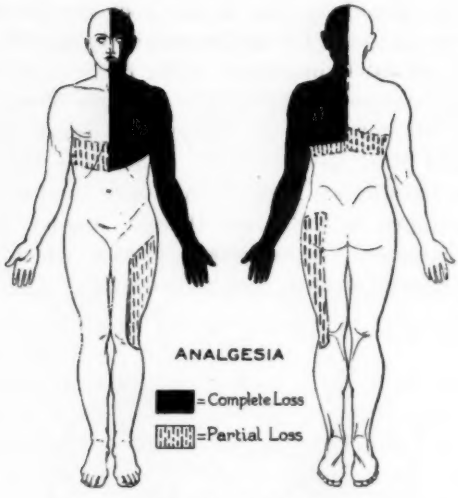


FIG. 9B.—Case II. Analgesia in 1902.

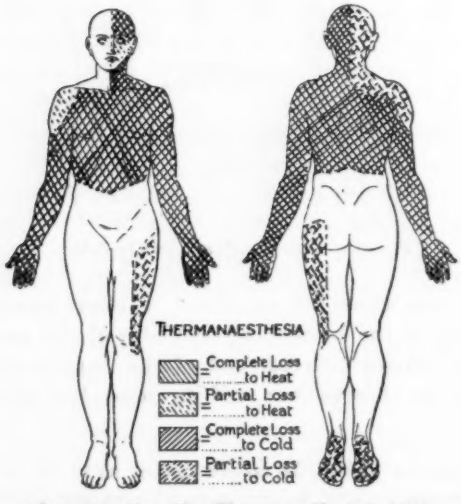


FIG. 9C.—Case II. Thermanæsthesia in 1902.

menced five years before, and was first noticed after she had had an abscess over the left first dorsal interosseous muscle. This abscess was opened without an anæsthetic, and the surgeon complimented her on her "pluck." But, as she laughingly observed, she deserved no credit, for the operation was absolutely painless! After this she began to have "pins and needles" in her left hand, which gradually spread up to her shoulder. Numbness was superadded, and in 1901 muscular weakness and contraction of the hand developed. She was admitted to the hospital in 1902. Apart from the weakness of the arm and hand and the anæsthesia shown in the charts (figs. 9 A, B, and C), nothing was noted except marked nystagmoid jerking of the eyeballs. She remained in hospital for two months, and was afterwards for a time at the convalescent home. There was no difficulty, even in the out-patient room, in making a diagnosis of syringomyelia, and examination in hospital confirmed the out-patient diagnosis. There was nothing significant in her personal history or family history, except that a sister had died of probably disseminated sclerosis.

FIG. 10.—Case II. Showing scoliosis in 1905.

She was re-admitted to the hospital in 1905 and then she complained of weakness of the left leg as well as of the left arm. There was no wasting of the leg muscles, but there was an exaggerated knee-jerk on this side and also ankle-clonus. A definite lateral curvature of the spine had now developed (fig. 10). The left hand was a characteristic *main en griffe*, but the wasting was masked to a great extent by what has been described as a "succulent" appearance of the back of the hand and fingers (figs. 11 and 12); there was a

purplish redness and an appearance as if the hand were cold, although to the touch it felt quite warm. The wasting had spread up the left arm to affect the muscles of the shoulder-girdle, and there was also some wasting of the muscles of the right shoulder. The nystagmus was more marked than before, but the sensory condition was little changed.

FIG. 11.—Case II. Patient in 1905.

FIG. 12.—Case II. Showing swollen appearance of the left hand.

She was again admitted on May 15, 1909. The weakness in the left arm and leg had increased and there was wasting in the left calf. The plantar reflex was now extensor on both sides, and she complained of numbness of the whole of the left side. There was some unsteadiness in standing and a little difficulty in passing urine. The trophic change in the left hand was now

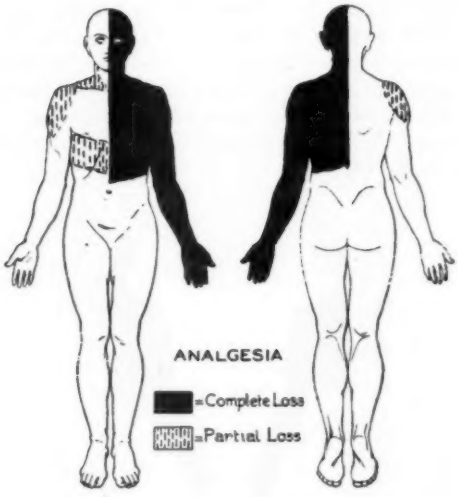


FIG. 13A.—Case II. Analgesia in 1909.

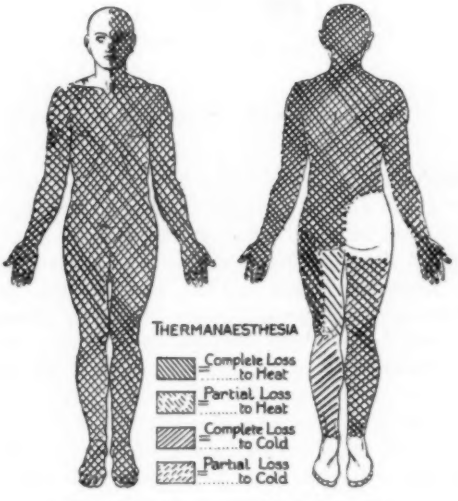


FIG. 13B.—Thermanæsthesia in 1909

more marked; the hand was swollen and of a purplish red colour all over. The sensory changes are shown in the diagram (figs. 13 A and B). She was again admitted on February 22, 1911. There was no marked change except that there was now slight wasting of the right hand, partial ptosis of the left eyelid, more marked nystagmus, and greater weakness of the lower extremities with increased spasticity of them. She had on this occasion a discharging painless boil on the right buttock; she also complained of some difficulty in articulating, although this was not noticeable. The analgesia recorded on this occasion is shown in fig. 14.

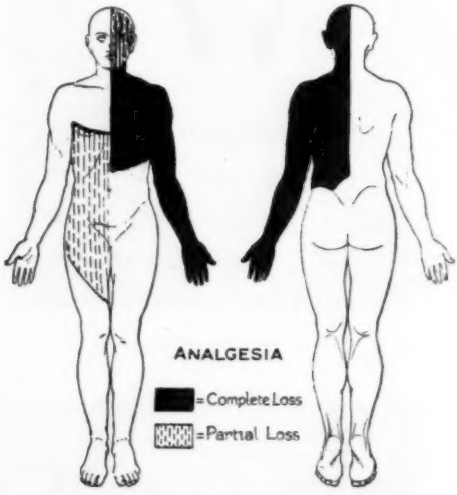


FIG. 14.—Case II. Analgesia in 1911.

She was in hospital also in 1916 but no change of consequence seems to have been noted. Her weakness in the upper limbs had increased and there was greater difficulty in walking. She was more pale and anæmic than before. There was no marked alteration in the condition of sensation.

On admission again, on March 3, 1919, her condition was one of great helplessness. She was quite unable to get about on account of the great weakness of the lower limbs, which she could only move a little in bed. Her left arm was powerless and her right almost as weak. She could not raise her head from the pillow. The nystagmus was marked and very coarse, and she complained that objects always seemed to be dancing up and down. The wasting was general but more marked on the left side; it included the sterno-mastoids and erectores spinæ. The knee-jerks and ankle-jerks were still active; there was bilateral ankle-clonus and each plantar reflex was extensor. The abdominal reflexes were absent, and there was some difficulty in passing

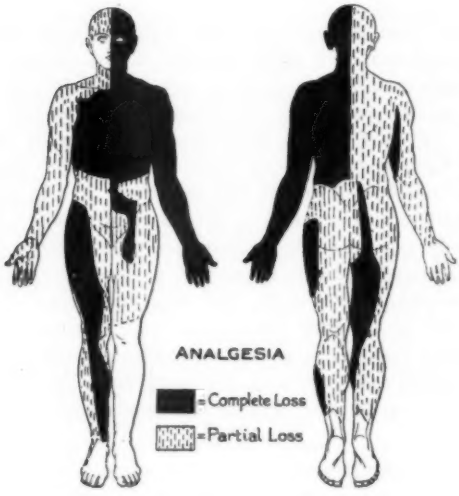


FIG. 15A.—Case II. Analgesia in 1919.

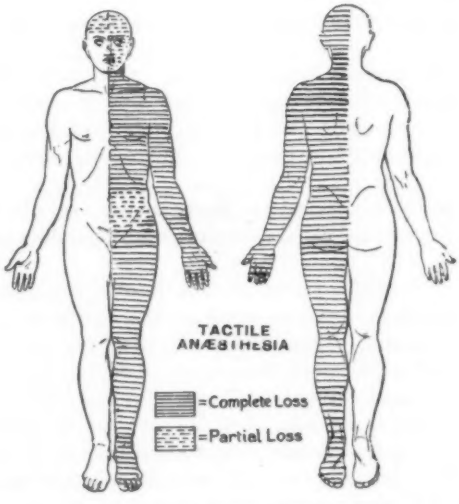


FIG. 15B.—Tactile anæsthesia in 1919.

urine. The sensory changes then present are represented in figs. 15 A and B. She was sent to the Convalescent Home at Finchley, where she died on April 13, 1921.

We have here, then, a case of a girl with nothing significant in her personal history, and the only point to note in the family was the possible occurrence of disseminated sclerosis in a sister. At the age of 17 she had a painless abscess on the left hand, the evacuation of which by incision was also unattended by pain. The subjective sensation of numbness in the left hand which was experienced a year later, in the course of four or five years spread up the left arm to the shoulder. At the age of 22, i.e., five years after the first symptoms appeared, she came under observation with wasting of the left arm and the disturbance of sensation depicted in the charts. From this time onwards there was a slow but steady extension of the numbness, wasting and weakness, with signs indicating involvement of the lateral columns and of the fifth cranial nerves. The muscular wasting and consequent weakness resulted in almost complete immobility of the limbs and trunk, and the sensory impairment also extended. Death occurred at the age of 42, twenty-five years after the commencement of the illness.

Pathological Examination.

A post-mortem examination was made on April 14, 1921.

The body was generally emaciated, but there was especially severe wasting of both upper limbs, perhaps rather greater on the right side than the left. There was a recent acute bed-sore over the back of the right shoulder.

The brain and cord were removed and suspended in 10 per cent. formalin saline.

The brain was abnormally long, measuring 19 cm. in length and 14 cm. in width. There was a slight degree of hydrocephalus, the anterior and posterior horns of the ventricles being about 2 cm. wide and having rounded tips. Apart from this the brain showed no gross abnormality above the level of the medulla.

The cord in the lower cervical and upper thoracic regions was a very thin-walled tube, filling the spinal canal and containing clear fluid like cerebrospinal fluid.

After fixation in formalin pieces from each of the segments of the cord were placed in Weigert's primary mordant, the cavity in them being filled with threads of pyroxylin. These dissolved out during the further processes of embedding in celloidin, leaving rings of spinal cord in much the shape that they would have assumed during life. Transverse sections from the mid-brain, pons, and medulla (the lower part of which was cut in serial sections), and from each of the spinal segments, were stained both by the Kultschitsky-Pal method, and by alum-hæmatoxylin with van Gieson's counterstain.

Pieces of the left ulnar nerve and a branch of the median (probably a sensory branch), and of the flexor sublimis digitorum and flexor carpi ulnaris

muscles were also taken out and fixed in 10 per cent. formalin saline. The nerves were treated by the Weigert-Pal (Kultschitsky-Pal) and Marchi-Busch methods, and the muscles embedded in celloidin and sections stained with hæmatoxylin and van Gieson's counterstain.

The cavity.—The actual cavity extended from the middle of the medulla down to the upper border of the third lumbar segment. In the medulla it took the form of an irregular oblique slit which passed from the middle line of the floor of the fourth ventricle forwards and to the left towards the line of emergence of the ninth, tenth and eleventh left cranial nerves. In the upper cervical cord the slit extended through the grey matter of the dorsal horns and grey commissure, from the entrance of the posterior roots on one side to the corresponding point on the other side, being at some levels continuous with the central canal of the cord, at others separate from it. In the middle cervical region the cavity quickly widened and the cord from that level down to the lower end of the thoracic region was hollowed out into a tube; the width was greatest and the walls were thinnest in the cervical enlargement, and the tube gradually narrowed as it passed down through the thoracic region as far as the seventh thoracic segment; here it began to dilate again, but at the first lumbar segment it closed down abruptly to a small transverse slit which hardly extended laterally beyond the grey commissure. Below this for two segments there was a dilated central canal, but in the third lumbar segment it was occluded and there was no cavity in the remainder of the cord.

In every microscopic section in which cavitation was present there appeared also an area of gliosis; it was nearly always in contact with the cavity, at some levels surrounding it entirely and being widest about its angles, so that the conclusion was irresistible that the cavity was formed by the splitting of gliosed tissue and subsequent widening of the split by breaking down of its walls.

Occasionally small isolated areas of gliosis were found in the white matter, especially between dorsal columns (fig. 21), but on the whole it appeared that the gliosis-cavitation process overcame the grey matter with greater ease than the white; at many levels the grey matter was almost entirely eroded while a considerable amount of white remained, and, moreover, when the cavity came to the surface of the cord, as it often did, it generally did so along the lines of the posterior horns.

Changes in the medulla :—

Gliosis was carefully sought for in all parts of the central nervous system. No trace of it was found in the cerebral hemispheres, mid-brain, pons or upper medulla; its upper limit was in the medulla about the cerebral end of the hypoglossal nucleus, but this level was not accurately determined. At the level of the tip of the calamus scriptorius the morbid change was extensive and the oblique slit already mentioned was present (fig. 16). In the middle line there was an extension of the cavity of the ventricle between the hypoglossal nuclei. On the left side the slit passed almost to the periphery, following roughly the line of the tenth nerve roots, and not

only was all the area behind it more or less degenerated, but it would appear from comparison with the right side that there had been considerable loss of tissue. The most dorsal part of the twelfth nucleus, the dorsal bundle of Schütz and the dorsal nucleus of the tenth and eleventh nerves, having lain in the line of the slit, were missing, and the descending nucleus of the trigeminus could not be distinguished. Dorsal to the slit the nuclei of the posterior columns were destroyed by gliosis, and the fasciculus solitarius showed degeneration and was devoid of surrounding cells. The area of the pyramidal tract was pale on both sides, especially on the right, some of its fibres having degenerated up to this level (retrograde degeneration). Emerging fibres of the hypoglossal nerve were fewer on the left than on the right, and though the nucleus of the nerve showed no gliosis it was deficient in cells.

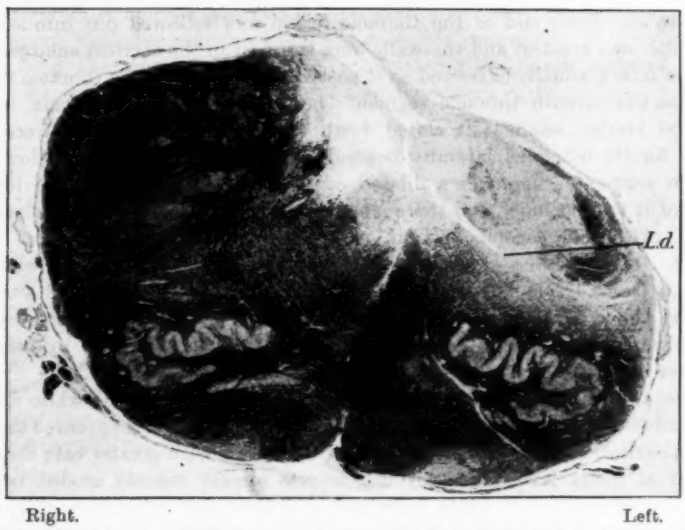
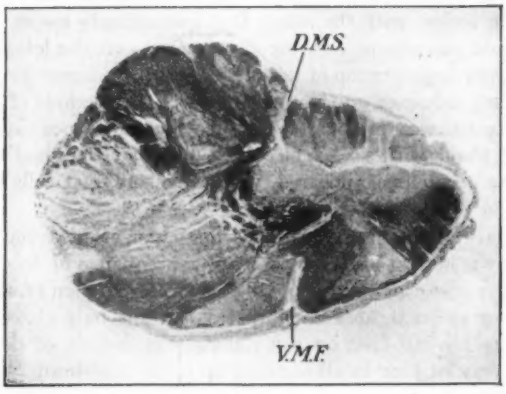


FIG. 16.—The right mesial fillet is severely degenerated, and the left fasciculus solitarius has almost disappeared. *L.d.*, Lateral diverticulum or slit.

In the lowest part of the medulla (fig. 17) the amount of gliosed tissue was much smaller relative to the cavity than at the level of the calamus, and at the decussation of the pyramids the loss of tissue on the left side of the medulla had been so great that this side was only about one-third the size of its fellow. The slit had inclined ventrally on attaining this level and had reached the periphery on the left, while in front of it a column of gliosis had formed round the central canal. By the erosion on the left side the left pyramidal tract had been completely destroyed just after it crossed, and by



Right. Left

FIG. 17.—The whole of the right pyramid and the lateral part of the left are degenerated. The internal arcuate fibres coming from the right dorsal column nuclei stain normally, but those from the left have disappeared. *D.M.S.*, dorsal median septum, *V.M.F.*, ventral median fissure.

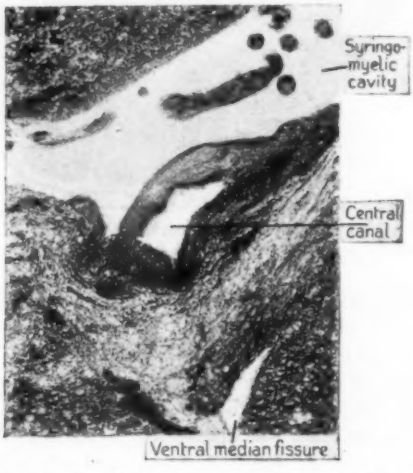


FIG. 18.—Case II. Cord at level of second cervical segment.

the gliosis round the central canal those fibres of the right pyramidal tract which had lain most posteriorly in the decussation were also interrupted. The interrupted fibres on both sides evidently degenerated both upwards and downwards from the lesion, with the result that immediately above its decussation the right pyramid was almost entirely degenerated and the left pyramid at the same level showed degeneration of its lateral part; the descending degeneration had an important influence on the appearance of the sections of the cord.

No central canal was present at this level but in its position there was an area of gliosed tissue with a large circular clump of ependymal cells. A little lower down, the canal itself appeared, with the ependymal cells quite regularly arranged around it (fig. 18).

These primary lesions gave rise to other changes of a secondary nature both at their own and at other levels. A consequence of the destruction of the nuclei of the posterior columns and of the interposition of the slit was the total absence of internal arcuate fibres in the left half of the medulla and therefore of the median fillet on the right: this default of the fillet on the right side was very striking in all sections up to the mid-brain. At the level of the calamus, the area from which the fillet had disappeared seemed to have shrunk, drawing forward the tecto-spinal and posterior longitudinal bundles (fig. 16).

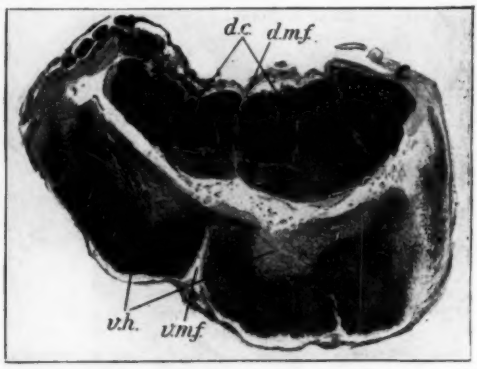


FIG. 19.—Case II. Cord at level of third cervical segment. *d.c.*, Dorsal columns; *d.m.f.*, dorsal median septum; *v.h.*, ventral horns; *v.m.f.*, ventral median fissure.

Another consequence of the interruption of the arcuate fibres was that the restiform body on the left side was much smaller than that on the right; in fact the left side of the medulla as a whole was smaller.

The ventral and probably the dorsal cerebellar tracts were degenerated both at this level and above. On the left side too, above the level of the disease, the rubro-spinal tract was degenerated (retrograde).

The spinal cord.—In the upper cervical sections (fig. 19) a wide fissure swept right across in an arc from the entrance of the posterior roots on the

left to the pyramidal tract on the right, reaching the periphery at both sides. Lying ventral to it in the middle line was the column of gliosis seen in the lower medulla, with the central canal now beginning to appear in it. Of the grey matter only the ventral horns and the tip of the right dorsal horn remained. The left pyramidal tract was represented only by a few fibres and the right pyramidal tract showed extensive degeneration; the dorsal columns of the left side were small, especially that of Burdach; on the right

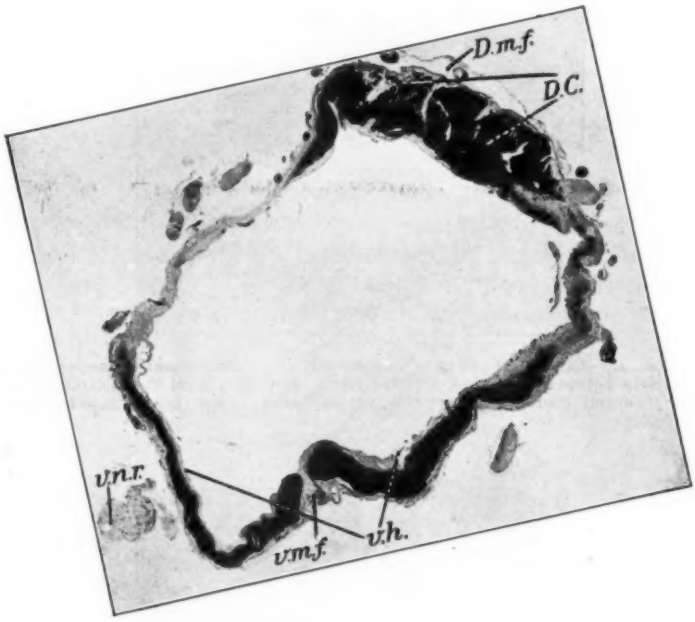


FIG. 20.—Case II. Cord at level of the cervical enlargement. *D.C.*, dorsal columns. *D.m.f.*, dorsal median septum; *v.h.*, ventral horns; *v.n.r.*, ventral roots; *v.m.f.*, ventral median fissure.

side the ventral part of the column of Goll showed considerable gliosis; the ventro-median columns of both sides and the ventro-lateral of the left had undergone partial secondary degeneration.

Passing downwards, the central canal first widened and then became continuous with the cavity. It was surrounded by a large number of cells, apparently ependymal, and the ependyma formed a lining for part of the ventral wall of the cavity. The cavity in the fourth cervical segment extended on both sides along the lines of the dorsal horns but did not quite reach the

periphery. At the edges of the cavity large numbers of cells were present but they did not form a boundary or lining; they were apparently glial.

In the cervical enlargement (fig. 20), the sections were irregular rings, the sides of which were formed chiefly by portions of the ventral and dorsal columns; the left pyramidal tract was completely degenerated and the right extensively but not completely so. Very small portions of the ventral horns were present.

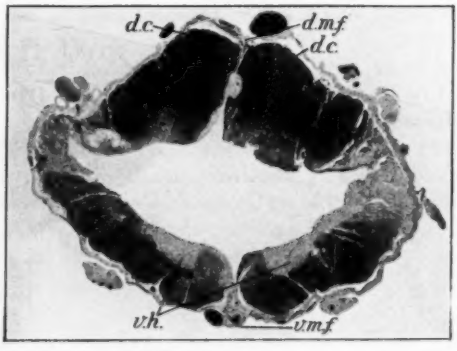


FIG. 21.—Case II. Cord in mid-thoracic region. *d.c.*, Dorsal columns; the pale oval area between them is a patch of gliosis extending from the central disease; *d.m.f.*, dorsal median septum; *v.h.*, ventral horns; *v.m.f.*, ventral median fissure.

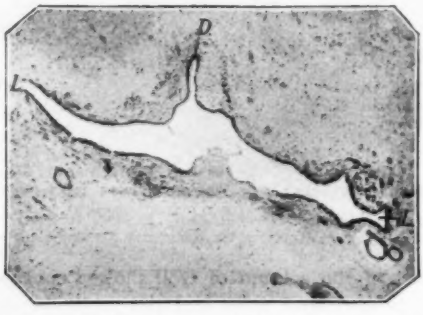


FIG. 22.—Case II. Dilated central canal at level of second lumbar segment. *D.*, Dorsal extension; *L.*, lateral extension.

Much the same may be said of the thoracic cord, but the ventral and dorsal columns were more compact, and the ring being smaller its walls were thicker. A greater part of the ventral horns persisted. More gliosed

tissue remained round the cavity, and at various levels the gliosis extended backwards between relatively healthy dorsal columns (fig. 21).

At the first lumbar segment the cavity, as has been said, narrowed quickly and appeared almost like a transversely dilated central canal. Its ependymal lining was not, however, complete, and it was surrounded by a zone of glial tissue containing a large number of cells which were ependymal in nature. The same appearances prevailed down to the third lumbar segment (fig. 22).

The outline of the cavity in the lumbar cord is particularly interesting, first, since it is similar to that of a stage of the developing canal, and secondly because a cavity of just this shape prolonged a little to one side, as it was in the first lumbar segment, would interrupt the crossing pain and temperature fibres from that side without affecting the touch fibres going to the dorsal column, and so produce a unilateral dissociated anæsthesia. A similar extension to the other side or a slight extension forwards would make the sensory loss

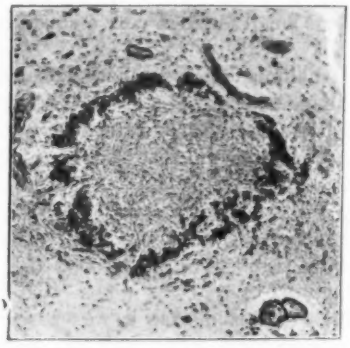


FIG. 23.—Case II. Section of fourth sacral segment ; ring of ependymal cells surrounding a pencil of glial tissue. Note the clear zones around the vessels.

symmetrical. One imagines that such a lesion if placed in the cervical cord might, in the absence of any interruption higher up, be the cause of the dissociated sensory loss in one arm, which was the first symptom.

The cavity was completely closed at the third lumbar segment. In the rest of the cord a slender pencil of finely reticular substance occupied the site of the central canal, containing irregular clumps of ependymal cells ; in the lowest segments these were arranged in a fairly regular ring around it (fig. 23).

Wherever gliosis or cavitation was seen, the large number and size of the vessels in and around the affected parts was noticeable; often they were actually free within the cavity. Apparently the vessels were more resistant to the process of gliosis and erosion than the nervous elements, with the result that those from the destroyed areas came together near the cavity.

The vessels which lay in or near an area of gliosis, but still surrounded by compact tissue, were usually encircled by a small pale-staining, translucent zone or by a small clear space; this appearance was best seen in the lower parts of the cord (fig. 23). This feature has been described by Schlesinger and by others.

Peripheral nerves.—Sections of the branch of the left median nerve showed no abnormality either by the Weigert-Pal or Marchi-Busch methods. The left ulnar nerve on the other hand showed gross degeneration. In sections stained by the Weigert-Pal method with van Gieson's counterstain, many of the nerve bundles showed no trace of myelinated fibres. In others there were small collections of fatty droplets which stained more deeply by the Weigert-Pal than the Marchi method; they appeared to be collections of altered myelin in the bodies of phagocytic cells and were evidence that some of the nerve degeneration had taken place at a comparatively recent date. Here and there were bundles of fibres which retained some myelin sheaths, but in most of these the proportion of fine to coarse myelin sheaths was very much greater than the normal. In some small bundles only a single myelinated fibre could be seen.

Muscles.—The flexor sublimis digitorum showed changes typical of a muscle which has degenerated in consequence of a lesion of its motor nerve. In cross sections some fibres appeared of nearly normal size, but their outline was rounded and in many the centre of the fibre stained palely. Other fibres were much smaller than normal; their shape was irregularly polygonal with rounded edges, and the nuclei of the sarcolemma sheath were increased in number and often had penetrated into the interior of the fibre. The muscle spindles and some of the nerve bundles in their neighbourhood (i.e., presumably sensory nerve fibres) appeared normal.

In longitudinal sections of this muscle it was possible to make out transverse striation in most of the fibres, but it was less well marked than normal, and in some of the fibres was almost invisible. Chains of nuclei running in or between the muscle fibres were very common, and most of the fibres showed an excessive number of nuclei within the sarcolemma sheath. In many places there were clusters of darkly staining nuclei lying between the muscle fibres.

In the flexor carpi ulnaris the changes were more varied, some bundles of fibres being comparatively healthy, others presenting an appearance similar to that seen in the flexor sublimis digitorum, and still others showing a later stage of the process of degeneration. In these the muscular tissue was represented by thin fibres with no sign of cross striation, containing chains of darkly staining nuclei which constituted the greater part of the substance of the muscle fibre. Transverse sections of this muscle showed in contiguous areas these three types of degeneration, and some bundles of partially degenerated fibres were surrounded by fibres which had degenerated completely.

Here, as in the flexor sublimis, the muscle spindles were healthy.

Relationship of Pathological Anatomy to Symptoms.

With such extensive destruction it is almost impossible to draw conclusions as to the causation of symptoms. A suggestion has been made already to explain the unilateral sensory loss by which the disease first manifested itself, but at the stage at which the patient died many pathological factors were at hand to account for her almost complete anæsthesia: as interruption of the spinal commissure throughout the cord, destruction of the dorsal root zone, lesions in the dorsal columns or their nuclei, and possibly destruction of the left spino-thalamic tract.

The weakness and wasting of the muscles of the neck and upper limbs, and the trophic disturbances in the latter, are explained by the extensive destruction of the ventral horns in the cervical and first thoracic segments. The spastic paralysis of the lower limbs was obviously due to the degeneration of the pyramidal tracts.

The dysarthria must be associated with the partial destruction of the left vagal and hypoglossal nuclei.

The complete sensory loss on the left side of the face and absence of the left corneal reflex may be referred to the lesion of the descending root of the left trigeminal nerve; that sensation was lost on both sides on the scalp and forehead considerably earlier than round the nose and mouth is explained by the fact that the descending fibres of the first division of the trigeminal nerve end at a lower level than those of the second and third divisions [11] [14]. It is stated that the fibres of the first division lie ventro-medial to those of the second and third divisions, and in sections just above the lesion the more ventrally placed fibres were pale, especially on the left side.

The smallness of the pupils and the partial ptosis of left upper eyelid are accounted for by destruction of the sympathetic centres in the cervical or upper thoracic cord.

The nystagmus is not so easy to explain. Liedler [7], from pathological and experimental evidence, concluded that nystagmus in syringobulbia is due either to a lesion of the descending vestibular nucleus of one side, or to interruption by the fissure of fibres passing from this nucleus to the posterior longitudinal bundle of the opposite side, and his view has been supported by Levy-Suhl [6]. In this case, however, no lesion of the descending vestibular nucleus was seen, and although a careful examination revealed no difference between the posterior longitudinal bundles, some of the fibres passing to them from the left vestibular nucleus must have been interrupted.

A comparison of these two cases from the pathological aspect reveals radical differences in some respects in spite of a close similarity in others.

The most striking contrast is in the relationship of the cavitation to the process of gliosis. In Case I there was much more gliosis than cavitation. For example, the lesion in the medulla appeared to be almost altogether due to gliosis, and very little cavity formation had taken place in that region. And in the cord also the amount of gliosis was everywhere much more extensive than the cavity, which, over almost the whole of its extent, was bounded by a thick wall of glial tissue. In Case II, on the other hand, the most prominent feature was the cavitation. In the medulla relatively little gliosis was seen, and, although lower down in the cord isolated areas of gliosis were present, they were small and insignificant in comparison to the size of the cavity.

This pathological difference may be correlated with the clinical histories: in Case I the morbid process ceased to progress about twenty years before the patient's death, for which it was scarcely responsible; whereas in Case II it continued active, rendering the patient gradually more helpless.

With the scanty knowledge that we possess as to the nature of the pathological process at work in this disease, the relationship of cause and effect cannot be definitely stated; but certain features presented by these two cases suggest a possible explanation of the arrest of the disease in the first case.

It has been noted that in Case II the ventricles were somewhat distended, the cervical cord swollen to considerably above its normal size, and the central canal in the lumbar region much dilated. In Case I, on the other hand, there was no evidence of hydrocephalus, but the iter of Sylvius was unusually large, and gave the appearance of having shrunk to the shape it presented in cross section during the process of fixation. Further, the thick concentric cuff of glial tissue which surrounded the cavity in the lower cervical and dorsal regions of the cord conveyed the impression that it had been formed in response to some tension or pressure from within the cavity. There is thus in both cases evidence that the cerebrospinal fluid in the ventricles and central canal of the cord was under abnormally high pressure, and that this was one of the factors leading to cavitation in the medulla and cord. In Case I either this pressure had fallen, or the glial tissue surrounding the cavity had become firm enough to withstand the destructive effects of the increased pressure.

It is usually taught, and is probably true, that the process of gliosis in syringomyelia is primary, and that it is the breaking down of the new-formed glial tissue which is responsible for the cavitation in the cord. But it must be remembered that glial tissue is in all probability endowed with a very slow rate of growth, and that although in the earlier stages of this process it is extremely fragile, in the later stages it is probably firmer than normal nervous tissue. Therefore, if the destructive process ceased for a time, the glial tissue might become firm enough to resist any further cavitation.

In Case I it is possible (and an examination of the cervical region of the cord bears out the suggestion) that the fluid had formed a channel by which it could escape into the subarachnoid space, and that the formation of this channel coincided with the arrest in the progress of the disease.

The association of syringomyelia with symptoms of increased intracranial pressure, such as headache and vomiting, has been observed by many authors. In some such cases the post-mortem examination has shown the existence of internal hydrocephalus. Such a case has been described by Grund [1]. This patient, the mother of four healthy children, commenced at the age of 24 to have headaches, which continued for nine years without the development of any other morbid symptoms. A year before her death they became worse, and were associated with giddiness and vomiting, and a little later weakness of the arms and paraplegic symptoms were added. Death occurred with Cheyne-Stokes respiration; indeed the whole symptomatology of the case suggested the diagnosis of intracranial tumour. The post-mortem examination, however, revealed no neoplasm, but hydrocephalus associated with syringomyelia and syringobulbia.

Hassin [2] has drawn attention to the increased pressure of the fluid within the cord in cases of syringomyelia. In such a case observed at operation the distended cord filled the theca, and no pulsation was seen in it. A slit made into the cord released clear fluid under great pressure and the pulsation in the cord was restored. In commenting on this case he makes the suggestion that the thickening so constantly found in the walls of the vessels in and around a syringomyelic cavity is a process of compensation for the increased pressure outside them.

The conception that increased intracranial pressure transmitted to the cerebrospinal fluid may be a dominant factor in the causation of syringomyelia is in some ways allied to the well-known theory of

Langhans [5]. He observed in four cases the association of syringomyelic cavities in the cord with tumours in the posterior cranial fossa, and considered that the latter by compressing the vertebral veins led to venous stasis and œdema in the cord, with consequent distension of the central canal and disintegration of the grey matter. This theory serves to explain not only cases such as those which Langhans studied, but also those in which cavities develop in the cord below the level at which it is compressed by a tumour.

And it is possible that a similar venous stasis may occur in the cases in which hydrocephalus is associated with syringomyelia, for the increased intracranial tension may push down the lower part of the cerebellum through the foramen magnum and thus compress the vertebral veins. A pressure cone of this kind was described by Grund [1] in the case he recorded, but it was probably a terminal phenomenon. It seems, however, unlikely that in the classical slowly progressive form of syringomyelia there is sufficient venous stasis within the cord to lead to cavitation. Nor is it common to find such cavitation in cases of cerebral tumour or hydrocephalus. Therefore, while it is possible that venous stasis may be one of the factors in the causation of syringomyelia it cannot be the chief or even an important one in the majority of cases.

Meningeal and arterial disease, by diminishing the blood supply to the central parts of the cord, may undoubtedly be the cause of cavitation in some cases. But in both our patients symptoms commenced before the age of twenty, and at the necropsy there was no evidence of meningeal thickening or arterial disease, except in relation to the cavities in the cord.

But there is evidence of another and probably more important ætiological factor in both of these cases, namely, a congenital instability of the glial tissue in the regions which the central canal of the cord occupies during fœtal life. In both cases the lesion in the dorso-lateral part of the medulla corresponded fairly closely to the lateral wing of the cavity which is formed during the primary flexure of the neural tube in this region. And in both cases there was also a ventral extension of the fourth ventricle similar to what is present before the fusion of the basal laminæ.

In the cervical cord in Case I the central gliosed area closely resembled the shape of the fœtal central canal, and lower down in the cord this area corresponded to its ventral and dorsal extensions. In Case II the central canal in the lumbar cord was an approximate

reproduction of the fœtal canal, except that an ingrowth of glial tissue had replaced the ventral extension between the basal laminæ. Other considerations, such as the abnormal shape of the head, which was present in Case II and which has been described in other cases, emphasize the probability that the disease has a congenital origin.

It is difficult to explain the origin of the cavitation in the ventral part of the medulla in Case I on any of these theories. The clinical record suggested that this occurred at an early stage of the disease. In fact diplopia from weakness of the right sixth cranial nerve was the earliest symptom. Cavitation in this region is not common in syringobulbia, but has been recorded by Krauss [3], Raymond and Philippe [8], Rosenblath [10], Wilson [13], Grund [1], Spiller [12], and Rhein [9]. In the case described by Krauss the cavity lay, as in Case I, between the olive and the inner accessory olive, destroying the fibres of the hypoglossus. And in several of the other cases the cavity followed more or less exactly the line of this nerve.

An examination of the development of the hypoglossus reveals the fact that at an early stage of development the nucleus of the nerve lies relatively much nearer to the ventral surface of the medulla than it does at maturity. Several tract systems come later to lie ventral to it, notably the pyramid, the olivo-cerebellar system and the median fillet. The hypoglossal nucleus is thus shifted dorsalwards and its root fibres come to lie between the olive with its transversely crossing fibres to the cerebellum, and the two longitudinal tracts which constitute the pyramid and the median fillet. The arrangement of these tracts and the dorsal migration of the hypoglossal nucleus may make the line of its fibres a zone of lowered resistance, or of unstable cellular equilibrium, and so may lead to cavitation in the few cases in which this occurs.

REFERENCES.

[1] Grund, G. "Zur Kenntnis der Syringomyelie," *Deutsch. Zeitschr. f. Nervenheilk.*, 1908, **34**, 304.

[2] Hassin, G. B. "A Contribution to the Histopathology and Histogenesis of Syringomyelia," *Archiv of Neurol. and Psychiat.*, 1920, **3**, 130.

[3] Krauss, Ed. "Ueber ein Fall von Syringomyelie," *Virchow's Archiv f. Pathol., Anatom. u. Physiol.*, 1885, **101**, 304.

[5] Langhans. "Ueber Höhlenbildung im Ruckenmarke infolge Blutstauung," *Virchow's Archiv*, 1881, **85**, 1.

[6] Levy-Suhl. "Zwei Fälle von Syringomyelie bzw. Syringobulbie mit Nystagmus," *Monatschr. f. Psychiatrie u. Neurolgie*," 1919, **45**, 51.

[7] Liedler. "Ueber d. Beziehungen der Syringomyelie bzw. Syringobulbie zum zentralen Vestibularis," *Zeitschr. f. Ohrenheilk.*, 1918, **76**, 211.

[8] RAYMOND and PHILIPPE. Quoted by SCHLESINGER.

[9] RHEIN, J. H. W. "Syringomyelia with Syringobulbia," *Journ. Med. Research*, 1908, **18**, 125.

[10] ROSENBLATH, W. "Zur Casuistic der Syringomyelie und Pachymeningitis cervicalis hypertrophica," *Deutsch. Archiv f. Klin. Med.*, 1893, **51**, 210.

[11] SCHLESINGER. "Die Syringomyelie," 1902.

[12] SPILLER, W. G. "Syringomyelia," *Brit. Med. Journ.*, 1906, **ii**, 1017.

[13] WILSON, S. A. K. "Un Cas de Syringomyélie et de Syringobulbie," *Rev. de Méd.*, 1904, 685.

[14] WINKLER. "Manuel de Neurologie," 1920, **1**, part ii.

A STUDY OF THE CEREBRAL FIBRE SYSTEMS BY MEANS OF A NEW MODIFICATION OF ANATOMICAL METHODS. THE LATERAL WALL OF THE THALAMUS AND THE SAGITTAL PORTION OF ITS CEREBRAL FIBRE SYSTEM.

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THE amount of knowledge accumulated respecting the functions of the nervous system, in so far as those functions manifest themselves in movements on the part of the organism, is very large. A great number of most complicated phases of normal and abnormal behaviour have been correctly observed and are clearly understood. Yet our knowledge respecting the essential structures underlying such phases of behaviour remains small in amount and indefinite in quality. The diagrammatic and semi-diagrammatic representations of the arrangement of a great number of nerve conduction pathways, current even in the best publications on the subject, testify to the scantiness of a knowledge gained by distant and indirect methods of observation. As a matter of fact, a number of such diagrams rest upon pure hypotheses which, in their turn, have been deduced from certain kinds of behaviour.

Even our best method for the study of continuous pathways in the central nerve system, the so-called Marchi degeneration method, has its peculiar limitations. From the experimental application of this method man is rigidly excluded. Yet similar as is the basic plan of structure of the nervous system in all vertebrates, the human nervous system differs in many respects from the brain of even the highest anthropoid ape. In proportion to the size of the body the human brain is very much larger in bulk; and this increase in bulk implies both a vastly increased number of neurons, and a vastly increased complexity in their arrangement.

The study of the conduction pathways in the human brain by means of the Marchi method requires a rather involved combination of favourable circumstances. The lesion must be very small; the person must die within a period of some three weeks after the occurrence of the

lesion, and there must be an opportunity for an autopsy. Such a combination of circumstances is sufficiently rare to make this excellent method of very limited application.

The opportunities for study offered by old lesions, in tissue stained by the Weigert method, are, of course, very much greater. Yet whatever stain is employed, the current methods of sectioning the tissue make its subsequent investigation a matter of extreme difficulty, and the results of such a study to a great extent uncertain. Except in a few situations the fibre tracts in the brain do not pursue any direction for more than a fraction of a millimetre. Owing to their sinuous course they are cut obliquely or irregularly no matter in which direction the section is made. What one sees in the best Weigert preparations of the brain is a beautifully variegated and almost hopeless picture constituted of millions of dots and streaks.

Careful dissection of properly hardened tissue, although the oldest, still remains one of the best methods at the disposal of the anatomist. In the dissection of the brain, however, one meets with certain dangers and difficulties. The chief danger is the fallacy into which one is almost certain to be led by habitual attempts to make microscopic deductions from macroscopic appearances. The greatest difficulty is that of retaining good records of the successive steps in the dissection. In the best photographs of such preparations most of the fine detail is utterly lost, while good drawings are rare, expensive and time-consuming. Yet unless many of the consecutive steps in the dissection of any one specimen are correctly recorded for subsequent study, criticism and comparison, the method, relatively crude as it is to begin with, must remain of correspondingly small value.

The modification of current anatomical methods to be described, obviates many of the difficulties and increases the certainty with which fibre tracts may be traced in the central nervous system. By means of current methods, the direction of lines and surfaces is inferred from the observation of points; by means of the modification to be described, points, lines and surfaces are directly observed. By the employment of this modification it has been possible to view a very large portion of an entire cerebral fibre system, such as the thalamic, pallio-pontine and others, each in a single section under the microscope; and to trace with comparative ease and exactness the course of bundles that have hitherto been represented only schematically.

Method and General Technique.

The method consists of two processes: (1) longitudinal sectioning and (2) serial dissections.

(1) Longitudinal sectioning is a method of preparing serial microscopic sections of any size in the plane of the course of a fibre-tract, or of an entire cerebral fibre system. The general technique will be given in this place, and the special steps to be taken in the preparation of sections of very large and complicated fibre systems will precede the description of each system.

The method may be employed in connection with a number of the ordinary stains and with either normal or pathological tissue.

(*a*) The particular fibre bundle or sheet is dissected out along the apparent course of its fibres. In well-fixed tissue such dissection is made comparatively easy by the use of the right kind of tools. In addition to the knife and scissors, the tools employed in the present work were small, spade-like, blunt-edged glass chisels, curved at an angle of about 100° at their ends. Such chisels are easily made in the Bunsen flame, and are very smooth and keep clean. Their curve enables one to get under the thinnest strand of fibres and to lift it out of its bed by leading the instrument along its under surface in the line of cleavage of the fibres. Such instruments, too, make it possible to reach fibre-strands in places which are inaccessible to a straight instrument without a serious distortion of the parts, such as the depth of the posterior and inferior extensions of the lateral ventricle.

(*b*) The detached strand is marked so that the relations which its several parts bore to the bed from which it was detached can be determined. A rough drawing accompanied by legends serves the purpose.

(*c*) The piece of tissue is placed on a numbered glass slide, the side in contact with the glass being carefully recorded. A pad of absorbent gauze, uniform or varying in thickness according as the tissue is of the same thickness throughout its extent or not, is placed upon the specimen, and is covered with a second glass slide of the same size as the first. This package is now tied with a strong string, the degree of pressure exerted in tying being such as to ensure the uniform application of the tissue to the glass slide on which it rests.

(*d*) If the Weigert-Pal stain is to be employed, the package is immersed in one of the mordanting solutions. There it remains for three or four days, or long enough for the tissue to retain its flat shape when the package is untied. It is then taken out of the solution,

untied, and the top slide and the gauze pad removed. The strand of tissue is lightly fastened with a thread to the slide on which it rests and immersed once more in the mordanting solution, where it remains for the necessary length of time

If it is intended to use a stain which requires no preliminary mordanting of the tissue, the process of flattening it permanently may be accomplished by the use of alcohol or of any other fixative agent.

(*e*) When the mordanting is completed the glass slide with the piece of tissue tied to it is removed from the solution, washed, and treated with the alcohol and the ether solutions in the usual way employed in the preparation of Weigert-Pal celloidin sections.

(*f*) A glass slide is covered with tin (not lead) foil, and fastened to it by bending the edges of the metal around those of the glass. The tinfoil should be about 0·5 mm. in thickness. Such foil may be spread over the glass so that its surface is perfectly smooth and even. An attempt to use the ordinary very thin foil is almost certain to result in the failure of the subsequent procedures. The tin-covered slide is placed in a celloidin solution with the tin up. The slide bearing the tissue is removed from the alcohol-ether solution; the thread which holds the tissue to the glass is untied, and the tissue is gently pushed off the old slide and placed on the tin surface of the slide in the celloidin solution.

The vessel containing the celloidin solution should have a flat bottom, and it should rest upon a horizontal surface. The amount of solution in the vessel should be such that when it reaches the necessary final consistency its surface should rise above the embedded tissue for a height of about 3 or 4 mm.

(*g*) When impregnation and embedding is completed, a cut is made through the thickness of the celloidin, passing around the tin-covered slide. A convenient instrument is passed under the edge of the slide, it is lifted out, and its celloidin surface is fastened to a wooden block in the usual way. With the block resting on a table, the relations of the whole are then the following, from top to bottom: glass slide, tinfoil, tissue, a generous layer of celloidin, wooden block.

The edges of the tin are now bent away from those of the glass slide and the latter is removed. An edge of the tin is then held against the side of a pencil, which is rolled over the surface of the embedded tissue in such a manner that it becomes wrapped in the tinfoil. The metal is thus removed from the adjoining tissue, leaving behind a surface as straight and polished as a mirror.

The preparation is treated with alcohol or with cedar oil, in the usual way.

(*h*) The block is adjusted in the microtome in such a manner that the first cut will shave off a complete section. This is relatively easy since the tissue presents a perfectly even surface. In the present investigation it was found convenient to set the long diameter of the block as parallel as possible to the edge of the microtome knife; on the whole, therefore, the sections were in the same plane as, and more or less at right angles to, the apparent course of the fibres. The layer of celloidin between the tissue and the block permits the sectioning of the entire piece without waste. In this manner it was possible to produce longitudinal sections of strands of tissue 10 cm. long, 3 or 4 mm. in width and less than 1 mm. in thickness.

If the apparent course of the fibres in the tissue is not their true course, the fact is immediately discovered in the stained section. In a true tract the fine bundles of fibres may be followed in one and the same section in their entire length by merely moving the slide along the platform of the microscope. When a bundle leaves the main tract its deviation in a large field of uniformly parallel bundles is detected with the greatest ease. Moreover, in such sections perforating bundles are seen with a remarkable degree of definition, the cross-sectioned areas standing out prominently amid a field of longitudinal fibres. An example of such a perforating bundle is the auditory tract, which is cut across in the sagittal sections of the lateral portion of the thalamus. Those who have looked for this tract in normal Weigert-Pal preparations generally fail to identify it.

(2) In the microscopic preparations just described, the course of the fibre-tracts is observed in the two possible directions on a plane surface. Thus, in the illustrations which follow, the direction of the fibre-bundles is either up and down, or from before backward, or partly the one and partly the other direction. In order to leave as little as possible to the uncertain processes of deduction, the third direction was supplied by Serial Dissections.

For these dissections formaldehyde-hardened tissue was used. After through fixation the brains were removed from the formaldehyde solution, wrapped in towels and placed in loosely-covered jars. After two or three months the brain-tissue, but slightly shrunken, became sufficiently tough to permit the most detailed dissection.

A record of each step in the dissection is obtained by pouring on the preparation molten wax which, on cooling, furnishes a mould into which is poured plaster of Paris. When the plaster has set the wax is melted out. In this way a series of faultless reproductions of the

several steps in the dissection of the hemisphere is obtained. The series may be as large as the investigator pleases. In the present study seventy-eight casts were made of as many steps in the dissection of one hemisphere; fifty-seven of another; only ten of a third; and so on. For the study of the relations of the parts, and for comparison with the microscopic sections, such a series is invaluable. The moulding and the casting require but little time and skill. The wax never sticks to the damp brain-tissue, and projecting parts are pulled out of the mould with little difficulty.

Special Technique for the Preparation of Longitudinal Microscopic Sections of the Sagittal Portion of the Thalamic Radiation.

A curved instrument is entered between the corpus callosum and the cingulum, and the entire cingulum convolution, from the para-terminal body to the hippocampus, is removed. The association sheets between the cingulum and the other convolutions are next cleared away, until the callosal fibres are seen covering the entire mesial aspect of the hemisphere as far below and behind as the parieto-occipital and anterior calcarine fissures.

The septum lucidum is removed, the anterior pillar of the fornix cut as low down as possible, and the band of the fornix pulled away from around the thalamus. Below that band is torn off, together with the hippocampus and a part of the uncus, a short distance in front of the receding angle of the temporal ventricle. The association-sheets in the small sulci of the cuneus are cleared away. The floor of the anterior and posterior limbs of the calcarine fissure is cut through. The lateral ventricle is thus everywhere opened.

The superficial fibres on the dorsal and anterior surfaces of the callosal band—the fibres which face the antero-superior border of the hemisphere—are lifted up strand after strand and pulled off the mesial aspect of the hemisphere which they cover. This is continued until the thickness of the cut border of the corpus callosum is reduced to about one-half. At this stage it is found that the fibres of the callosal band, when pulled upon, break off easily at their point of contact with the hemisphere. These are the perforating fibres, and the fact that they have been reached is an indication that above the line of their entrance into the hemisphere the thalamic fan has been exposed on the mesial surface.

The ventricular ependyma is peeled off everywhere, except in the

groove between the corpus callosum and the caudate nucleus and in that between the latter and the thalamus. In the former groove the ependyma is strongly adherent to the fasciculus subcallosus, a part of which may be torn away by an attempt to expose it; in the latter the ependyma is as strongly adherent to the stria terminalis.

In the posterior and inferior extensions of the ventricle the removal of the ependyma brings to view the fibres of the tapetum. This covering must be lifted with great care, especially in the inferior horn where it is very thin. Lateral to this layer, the entire expanse of the ventricle, except the narrow space around the thalamus which is occupied by the tail of the caudate nucleus, is carpeted by the fibres of the thalamic fan.

The instrument is now inserted into the substantia nigra and the thalamus separated from the fibres of the pes pedunculi. With the fan of the peduncular radiation as a lateral guide, the sagittally placed sheet of thalamic fibres is easily separated from the mesial aspect of the hemisphere in the frontal, parietal, and occipital regions. The expanded portion of the anterior commissure is a lateral guide in the separation of the thalamic sheet in the anterior half of the temporal ventricle. Lateral to the thalamic fibres in the posterior portion of the temporal and the lower half of the occipital ventricle is a layer of fibres converging towards the globus pallidus, and from this layer, too, the thalamic sheet is separable with ease.

The protruding mesial portion of the optic thalamus is now gradually torn away in the line of cleavage of the fibres, leaving a thickness of 5 or 6 mm. of its lateral wall.

The circumference of the large sheet thus obtained is serrated above, the serrations corresponding to the gyri and sulci at the superior border of the hemisphere. Below the circumference corresponds behind to the lower lip of the calcarine fissure; in front to the outer or lower portion of the hippocampal convolution. Still more anteriorly the gap in the outline of the circumference corresponds to the horizontal fissure, in front of which is the gyrus rectus.

The surface of the sheet which corresponds to the mesial aspect of the hemisphere is placed on a large slide, and the preparation treated as described under the heading of General Technique.

THE LATERAL WALL OF THE THALAMUS AND THE SAGITTAL PORTION OF ITS CEREBRAL FIBRE SYSTEM.

Fig. 1 was prepared practically from a single section. A few defects were corrected from four other sections. The size of these sections was nearly 13 by 9 cm. It is not possible to produce a single photomicrograph of an entire section of such size at a magnification at which the small bundles of fibres become visible. The alternative is to photograph or to draw the section in parts, and to put the fields thus reproduced together side by side in the proper order. For practical reasons the expedient of drawing was adopted. The Edinger epidiascope was used at a magnification of 25 diameters. The resulting huge drawing—1·8 by 2·3 metres—was then photographed and reduced to its present dimensions. The lines of the photograph were gone over with ink and the photograph bleached out.

The disadvantage of such an illustration is that although it gives a concrete idea of the general appearance of the stained section, the sharpness of its lines produces the impression of a diagram. Such an impression is true to the extent that each line in the drawing represents not a nerve-fibre, but a bundle of fibres in the section drawn. The advantages of such a drawing are the concreteness of the fairly correct idea of the appearance of the section which it furnishes, and the fact that it enables one to eliminate certain irrelevant features, such as the perforating bundles of the corpus callosum.

A number of photographs were taken from different parts of the sections employed in making the drawing, and some of these are reproduced in the illustrations. They serve the purpose of correcting the impression of the diagrammatic nature of the drawing. Such a correction is especially important in this case, since, as will be seen, the facts revealed in these longitudinal sections differ in several essential points from those of a number of investigators who based their conclusions on sections cut in the ordinary way.

In this study the Weigert-Pal stain has been used throughout. This stain furnishes no clue to the functional direction of a nerve-fibre. It is to be understood, therefore, that except where such a functional direction is explicitly stated, *it is nowhere implied in the forthcoming descriptions.*

The main bulk of the thalamic radiation has the general form of a fan open for about 300 degrees of a circle. The gap in the circle is the horizontal fissure. This fan is placed, on the whole, in a sagittal

direction. A detailed account of its relations to adjoining structure will appear in a special paper.

The division of the thalamic radiation into several peduncles has no anatomical foundation. Dejerine [4] called attention to this fact, and other investigators agreed with him that the term "peduncles," in connection with the thalamic radiation, is to be used for convenience only.

Although it is true that the bundles of fibres of the thalamic fan are nowhere separated to the extent of justifying a division into peduncles, yet the several parts of the fan are each marked by certain characteristic features. These will be described as they appear when the thalamic radiation is viewed on a sagittal plane.

The Temporal Thalamic Radiation.

This does not include the auditory tract, which, in these sections, appears as a bundle of transversely cut fibres (fig. 1, IV).

The anterior portion of the temporal thalamic radiation has been described by Arnold [1], and has since been known as the temporo-thalamic fasciculus of that author. Since its fibres are spread out over the wide expanse of the wall of the temporal ventricle, however, this part of the radiation can hardly be called a fasciculus. In their course these fibres describe a series of curves which cannot be entirely explained by the curved lateral outline of the ventricular wall. From their junction with the postero-inferior portion of the thalamus, they proceed forward in the lateral wall of the temporal cavity. At varying distances from the receding anterior angle of the ventricle the fibres curve mesially within the floor, and the most anterior reach the mesial wall. All these turn backward, some within the floor, others within the mesial wall, and proceed in a posterior direction (fig. 1, I). The reason for this singular curvature of the fibres is probably to be found in the forward growth of the temporal lobe after the thalamic elements in it have been laid down, a probability which awaits corroboration at the hands of the embryologist.

In the long posterior part of their course the temporal fibres are arranged in parallel, rather coarse bundles, which are similar in appearance to those of the occipital radiation (fig. 1, II).

Before their junction with the optic thalamus, for a space of about 3 mm., the temporal fibres pass through the striate body, through the tail of the caudate nucleus. Within the substance of the latter they

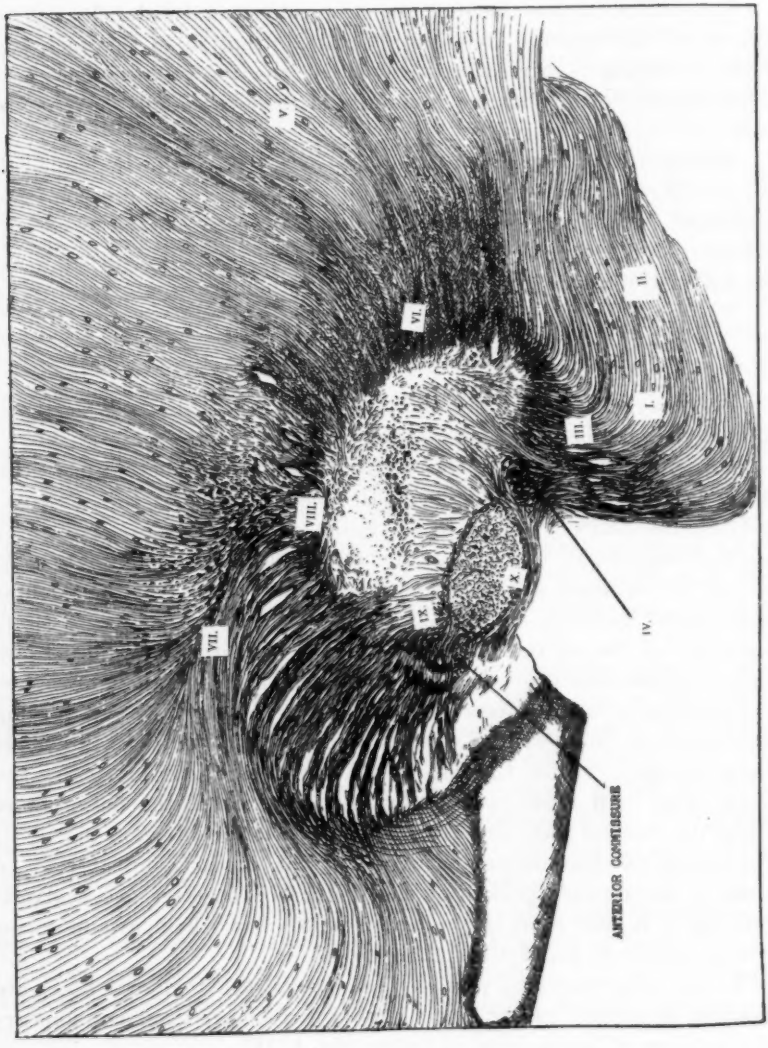

FIG. 1.—A drawing of the lateral wall of the thalamus and the sagittal portion of its cerebral fibre system. Details × 25.

are arranged in the form of flat bands, alternating with wide spaces occupied by the tissue of the striate body (fig. 1, III). The adjoining bundles show little tendency to interchange strands of fibres, as is the case in similar situations elsewhere, or to break up to any large extent into a brushwork of fibres similar to the brushwork to be described in connection with the occipital radiation. A number of fibre-bundles continue indeed distinct and parallel in an upward and backward direction until they have reached well into the outer middle portion of the nucleus of the pulvinar and the adjoining part of the lateral nucleus. That projection fibres from the temporal pallium stand (in the cat) in connection with the ventral region of the lateral nucleus, has been shown by E. Sachs [25] by means of experimental lesions. The nearly vertical course of the temporal fibres in the pulvinar gives that nucleus its characteristic streaked appearance.

Within the body of the thalamus most of the temporal fibres are situated immediately behind the auditory tract. This tract passes from side to side and is, therefore, cut across in these sections (fig. 1, IV). A smaller number of the temporal fibres, however, are placed in front of the auditory bundle, and are there intermingled with the fibres of a tract situated beneath the subthalamic body, which will be described later.

The Occipital Thalamic Radiation.

Two characteristics distinguish this portion of the thalamic system. For the greater part of their length the bundles, neatly arranged and parallel (fig. 1, V, and fig. 2), are coarser in texture than the other fibre bundles of the thalamic system. At a distance of about 2 cm. from the posterior surface of the thalamus, they begin to break up into their constituent fibres, appearing at first like a row of stiff feathers, but gradually, as they approach the thalamus, assuming the form of a soft, matted brushwork, with the general direction of the filaments toward the thalamus (fig. 1, VI). In the study of the fibre systems in the longitudinal sections, this phenomenon will be encountered over and over again. It is always significant of the proximity of the fibre bundles to the nuclear mass in which they disappear. As this feature is rather conducive to hasty deductions respecting the beginning or the ending of a fibre tract, it is important to visualize it and to understand it.

If the handle of a camel's-hair brush be taken to represent a compact bundle, then the brush itself will represent the part of the bundle

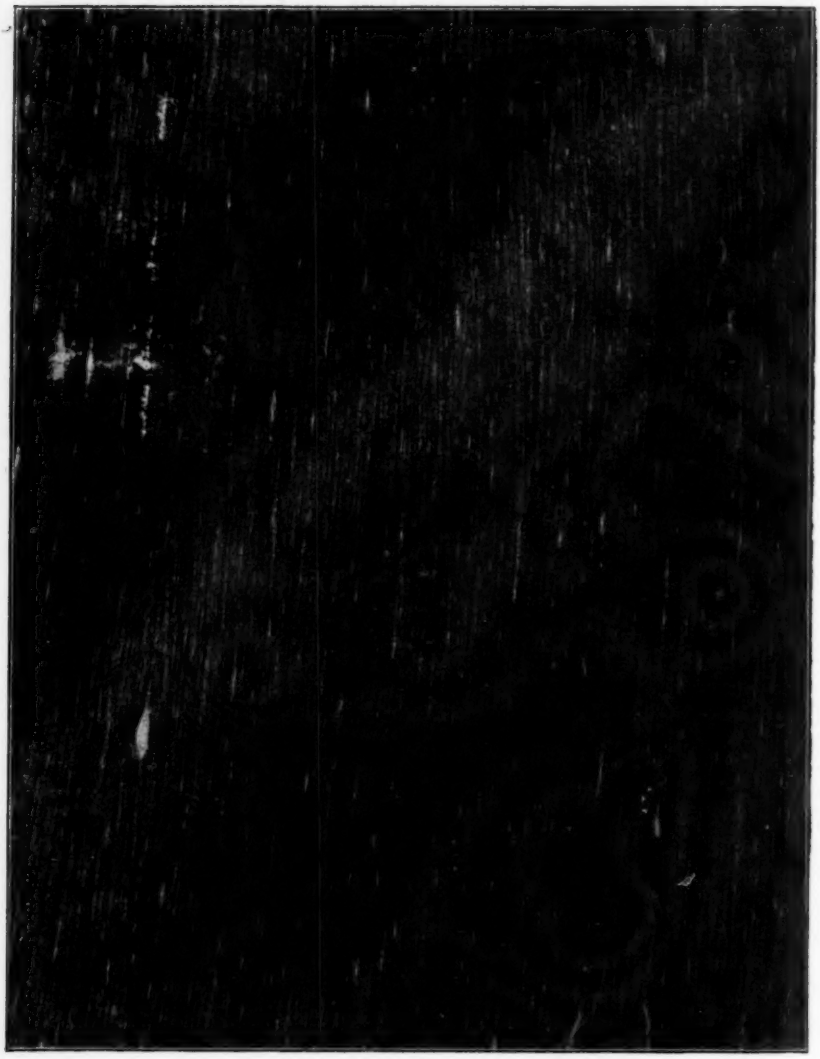

FIG. 2.—The occipital thalamic radiation. × 27.

where its fibres are spread more widely apart. If a number of such camel's-hair brushes, lying side by side, be embedded in paraffin or celloidin and then sectioned in the longitudinal plane, their appearance in each section will approximate that of the nerve bundles in fig. 1, VI.

In the neighbourhood of a nuclear mass in which a fibre tract begins or ends, its constituent fibres, gathered into compact bundles, must spread out. For this there are two reasons. One is that each cell is thicker than the fibre with which it stands in connection, and the entire nuclear mass, therefore, occupies a wider space than does the tract of fibres which it sends out or receives. The other is a rule which appears to hold good throughout the nervous system, central as well as peripheral, that there is a continual interchange of fibres between the adjoining bundles of a tract. That this arrangement holds good in the peripheral nerves, has been abundantly proved by the researches of Sherren [27], Heinemann [11], Langley and Hashimoto [13], McKinley [15], and a number of others. A careful inspection of the cerebral tracts shows that the finest parallel bundles which appear to retain a uniform thickness for a long part of their course, continually anastomose by means of very fine fibres, and that the whole tract is in reality a plexus of extreme intricacy. Owing to this it must be true that the mutual relations of the fibres in a nerve tract in the proximity of the nucleus in which it disappears are not the same as the mutual relations of the cells in the nucleus to which the fibres respectively belong. Thus of two fibres placed on the right of a nerve tract, one may pass to a cell on the right, the other to one on the left side of the nucleus. Hence the appearance of a matted brushwork of fibre bundles in the proximity of a nuclear mass to which they belong, seen in the longitudinal sections.

The phenomenon described, however, needs further investigation. It may be pointed out that in the neighbourhood of nuclei which are known to be efferent, such as the cranial and spinal motor nuclei, the emerging nerve-tracts are at first composed of parallel or converging fibres. In such nuclei each cell sends out but one nerve fibre, and these fibres then converge to form a nerve tract. There appears to be no reason for any matting of the fibres of an efferent bundle in the proximity of its nucleus, and none is observed. In the case of a tract near its nucleus of termination, however, the circumstances must be different. The fibres of that tract have changed places repeatedly, and in the neighbourhood of its nucleus each small bundle must break up into its constituent fibres, and the fibres must break up into thinner

fibrillæ, in order that each may come into relation with a number of cells or cell processes in different parts of the nuclear mass. Such a tract might be expected, therefore, to have the appearance of a matted brushwork near the nucleus which it is to enter. It may be said that for the same reasons a tract containing both afferent and efferent fibres might be expected to present a mixed appearance near the nucleus in which some of its fibres originate and in which others end. Such a mixed appearance should be clearly observable in sections cut along the course of such a tract. In the sections examined in connection with the present study, however, nothing but a mere suggestion of this appearance has been observed, and on that no conclusion can be based. The only certainty so far reached is that in the neighbourhood of the nuclear aggregate in which the fibres of a cerebral tract gradually disappear from view, the bundles of that tract are always seen in Weigert-Pal sections to assume the form of a matted brushwork. When examining the course of the prefrontal part of the thalamic radiation an opportunity will be presented for contrasting sharply the appearance of its smooth fibre-bundles near and within the thalamus with the matted brushwork of the other contingents in similar situations.

On joining the nucleus of the pulvinar the rich brushwork of fibres into which the parallel and well-defined bundles of the occipital radiation have spread out, gradually breaks up and disappears.

The Parietal Thalamic Radiation.

In sagittal longitudinal sections of the thalamic radiation this part always appears defective. In contrast to the pictures presented by the other contingents, that of the parietal is marred by a number of thick, short streaks (fig. 1). A certain number of fibre bundles bend away from the sagittal plane in a direction which is at first forward, upward and lateral. In their forward course these bundles contribute to the formation of the fasciculus subcallosus which will be described later. They then proceed further laterally, in an upward and backward direction. Owing to their lateral inclination they are cut in short strips in these sections. Their appearance is distinct from the rest of the parietal bundles; they are very much thicker and converge below at an unusually large angle, between 45° and 90°.

The general backward sweep of the parietal radiation, as well as the number of laterally inclined thick bundles which it contains, demar-

cate it rather sharply in front from the frontal portion of the thalamic fibres. Behind, however, it merges gradually into the occipital radiation.

At a distance a little over 1 cm. from the optic thalamus, the fibres of the parietal radiation become aggregated into rounded bundles some 2 or 3 mm. in thickness. The spaces between these bundles are occupied by the substance of the striate body, through which they pass on their way to the thalamus. These bundles will be further considered in the next section.

The Frontal Thalamic Radiation. The Fasciculus subcallosus. The Stria terminalis. The Fasciculus thalamo-temporalis arcuatus.

In dissections of the body of the lateral ventricle, a bundle of fibres may be seen lying in the groove between the head and body of the caudate nucleus below and the corpus callosum above (fig. 3). This bundle is most prominent over the dorsal portion of the head of the caudate; it thins out over the body of that nucleus and disappears at the beginning of its tail. In certain specimens it attains a thickness of 3 mm. from above downwards at its thickest part.

The extent to which the current methods of sectioning the brain are conducive to error is well illustrated by the conclusions reached respecting the nature of the subcallosal bundle by universally recognized authorities. One conclusion is that it serves as a connection between the cerebral cortex and the caudate nucleus; another, that it is an association tract between different parts of the caudate nucleus; a third, that it is a fronto-occipital association tract.

H. Sachs [26] states: "The most important bundle which unites the corpus striatum with the grey cortex . . . is the fasciculus nuclei caudati. This bundle accompanies the caudate nucleus, running parallel with it . . . on the lateral wall of the lateral ventricle. . . . Lateral to this bundle is the corona radiata of the internal capsule. . . . Posteriorly it diminishes in proportion to the diminution in the thickness of the caudate. . . . from the bundle fibres pass into the caudate and become lost there. It appears that this bundle is composed of fibres coming from the frontal and the parietal parts of the cerebrum, and from the insula."

Koelliker [12] sums up his conclusions as follows: "This bundle accompanies the caudate nucleus lengthwise, throughout its entire extent, ventral to the corpus callosum, and forms part of the lateral

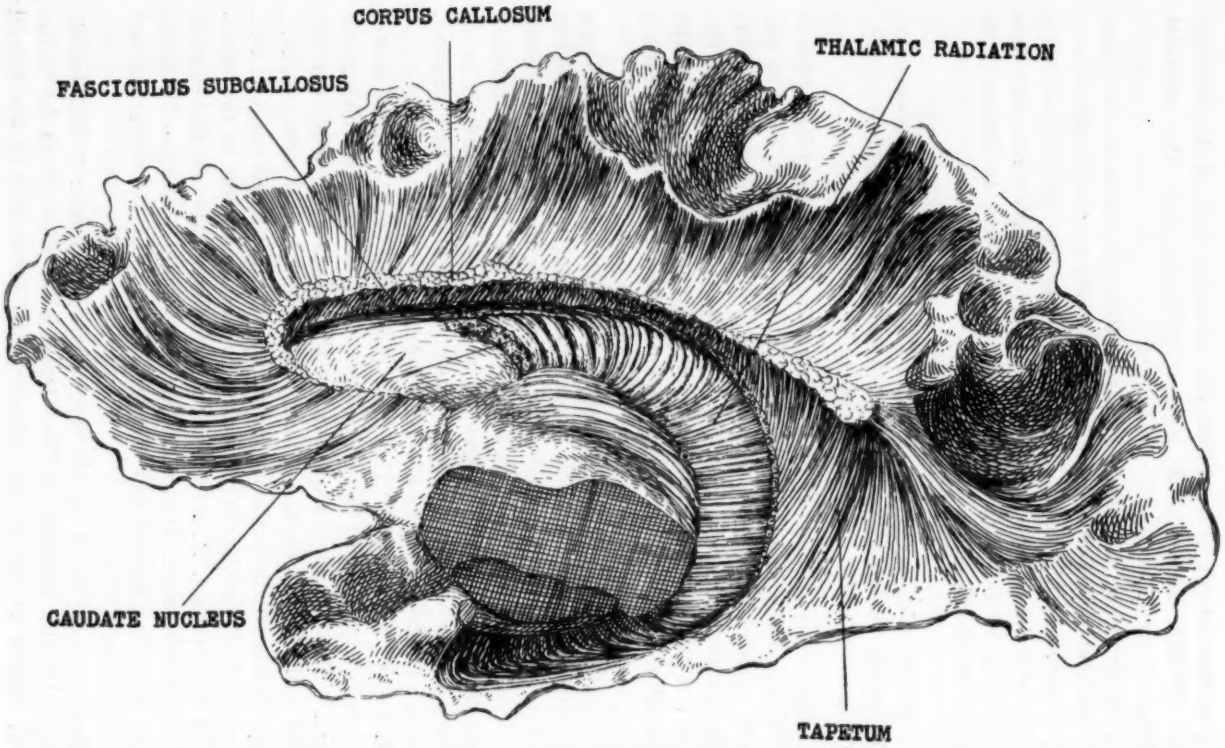

FIG. 3.—A drawing of a cast of a dissection on the mesial surface of the hemisphere. The body and tail of the caudate nucleus have been scraped away to expose the relations of the subcallosal bundle to the frontal and parietal bundles of the thalamus. A part of the tapetum has been cut away to show the course of the temporal and occipital thalamic bundles.

wall of the lateral ventricle. It diminishes in cross section from before backward. . . . Fibres enter the nucleus caudatus, where they become dispersed. . . . "

Edinger [6] devotes considerable attention to this bundle. "In mammals," he says, "there exists a small fibre tract which passes along the entire extent of the nucleus caudatus. It begins in front at the head of the ganglion as a few fibres which appear to come out of the head itself. This tract increases in size more and more posteriorly for a certain distance, then becomes smaller, in consequence of the slenderness of the tail of the nucleus. . . . The bundle lies in the angle between the nucleus caudatus and the roof of the ventricle; the fibres of the corpus callosum radiate over it. The fibres of this bundle appear to come from the nucleus itself and to return into it again. This is called the association bundle of the nucleus caudatus; but I cannot separate it sharply from the fronto-occipital association bundle which lies close to it."

Bechterew [2] is very emphatic in his statement that this bundle consists of fibres connecting the cortex with the caudate nucleus. He states that degeneration of that bundle is observed principally after lesions of the frontal and parietal lobes, and to a less extent in those of the occipital lobe. After destruction of the frontal lobe it was possible to observe the degenerated area diminish from before backward, which, he thinks, points to the fact that the fibres originating in the frontal region of the cortex end in succession from before backward in the caudate nucleus. In a footnote the author cites Flechsig as being of the same opinion.

Probst [20], however, was not able to find any considerable degeneration in the subcallosal bundle in isolated lesions of the caudate nucleus. After destruction of the bundle in the anterior parietal region, the fibres degenerated in his experiments for a short distance only, and he could not follow their ends with certainty. He states, however, that more extended degeneration of the fasciculus followed deep destruction of the posterior cerebral region.

In the sagittal sections of the thalamic fan prepared by the method of longitudinal sectioning, the subcallosal bundle stands out with the greatest degree of clearness possible with the Weigert-Pal stain. With the unaided eye, as well as with all degrees of magnification, the bundles of fibres composing it can be traced from the frontal and partly from the parietal regions of the hemisphere, through the substance of the

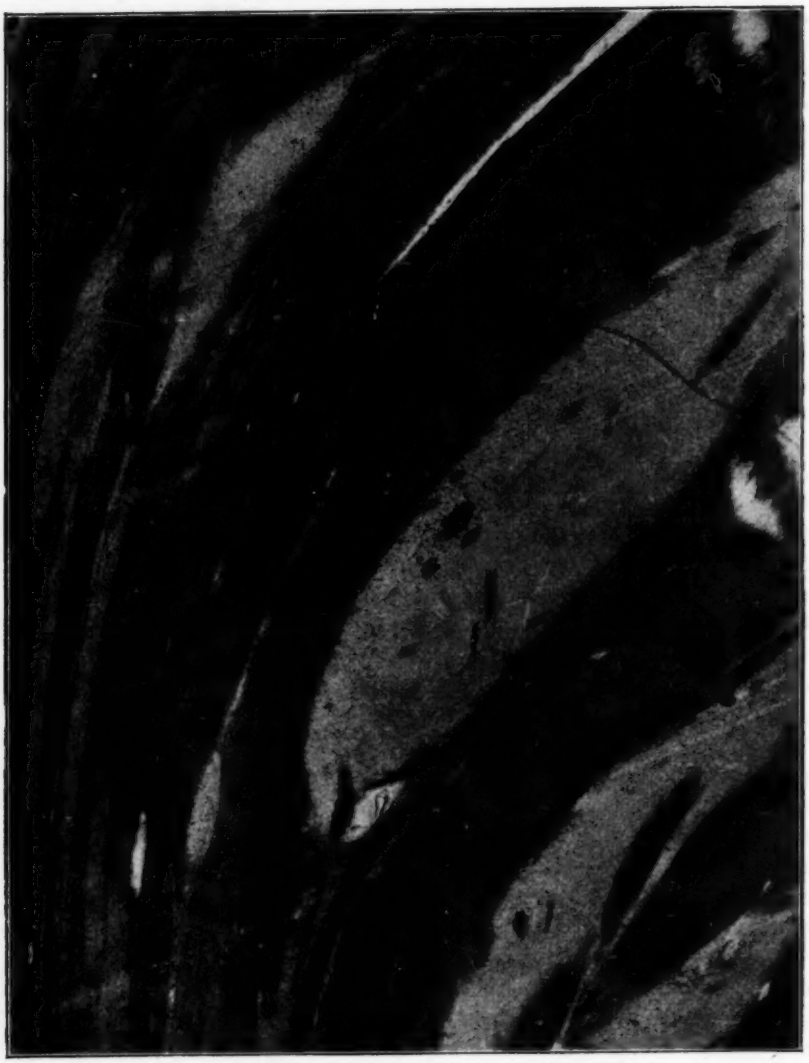

FIG. 4.—Fasciculus subcallosus. × 27. Above the direction of the bundles is almost horizontal. They are plainly seen to curve down, plunging through the substance of the caudate nucleus, on the way to the thalamus.

caudate nucleus, and into the optic thalamus. Fig. 1, VII, and fig. 3, indicate the course of the fibres composing the subcallosal fasciculus.

The fact is that the fibres between the frontal regions of the cortex and the thalamus pursue a rather intricate course. From in front and above they pass at first downward and backward in a series of graceful curves; they then all turn backwards in an almost horizontal direction over the head and body of the caudate nucleus. In the horizontal part of its course the entire mass of fibres is packed into a single bundle of considerable width. At various distances from before backward this horizontal band gives off five or six fasciculi, which turn downward and plunge through the substance of the caudate nucleus to join the thalamus in the region of the stria terminalis.

A vertical or a horizontal section of the hemisphere passing through the caudate nucleus shows that no part of it is sufficiently separated from the rest of the corpus striatum to allow it to be regarded as a separate ganglion. To the anatomists who have described the subcallosal bundle the fact was well known that the existence of the caudate nucleus as a separate entity is a mere gross appearance. The form of that nucleus—a thick head in front, a body and a thin tail behind—is due mainly to the fact that from a mesial viewpoint the smaller thalamus leaves exposed a greater portion of the striate body above and in front than it does behind and below. Nor is the separation of the exposed from the concealed part of the striate body at all accomplished by the stream of fibres which perforate that body.

Even if it were true, then, that the fibres of the subcallosal fasciculus stand in connection with the cells of the caudate nucleus, it still remains difficult to understand why the fasciculus diminishes in thickness posteriorly, in proportion to the diminution in the thickness of the caudate nucleus.

A case of agenesis of the corpus callosum in the microcephalic brain of an idiot, described by Onufrowitch [19] and later by Forel [7], is responsible for a conception of the nature of the subcallosal fasciculus which still prevails. Notwithstanding the absence of the callosal band in this case, the tapetum was intact in the posterior extension of the lateral ventricle. Onufrowitch and Forel thought, moreover, that the tapetum was continuous in front with a bundle of fibres which passed between the cingulum and the caudate nucleus to the frontal portion of the hemisphere. They, therefore, concluded that the tapetum was not part of the corpus callosum, but that, together with the bundle of fibres which they saw pass to the frontal portion of the hemisphere, it

constituted a fronto-occipital association tract. They called it the fronto-occipital fasciculus and identified it with the superior longitudinal or arcuate fasciculus described by Burdach.

Muratoff [18], in his experiments on dogs, found by the employment of the Marchi method that the amount of degeneration in the bundle described by Onufrowitch was relatively small when any single cortical area was injured. He also found traces of degeneration in it in lesions of the parietal cortex as well. He, therefore, disagreed with Onufrowitch that the bundle served to connect only the two areas implied by its name, and came to the conclusion that it was too complex in nature for any specific name and proposed to call it the fasciculus subcallosus. Respecting its identity with the superior longitudinal fasciculus of Burdach, he rightly pointed to the fact that the latter association tract is situated on the lateral side of the corona radiata, while the bundle in question is to be found on its mesial side.

Dejerine [4], using the same argument as did Muratoff, points out the error in identifying the subcallosal fasciculus with the superior longitudinal fasciculus of Burdach. He agrees with Onufrowitch and Forel that the subcallosal bundle is a fronto-occipital association tract. He brings, however, a number of facts to bear upon the nature of the tapetum, showing that it does contain a certain contingent of callosal fibres.

Wernicke [28] thought that the fasciculus in question was composed mainly of the fibres of the corpus callosum, but that it also contained a certain number of fibres from the frontal lobe. He declares, however, that he knows nothing further about its course.

That the subcallosal fasciculus is composed of fibres which extend into the large areas of the frontal and parietal cortex, has already been noted. When considering the course of the prefrontal and orbital fibres it will be seen that they curve for some distance upward around the head of the caudate nucleus, before plunging through its substance. In that situation, therefore, these fibres contribute to the formation of the anterior portion of the subcallosal bundle (fig. 1).

It can be easily understood that lesions of the occipital cortex would bring about degeneration of the fibres of the tapetum, if this is constituted either in whole or in part of callosal fibres. That lesions of the parietal and frontal regions of the cortex would result in degenerations in the subcallosal bundle is also easily understood. Yet that by no means implies the continuity of the frontal and parietal fibres with those of the tapetum. The difficulty lies in the obscure space which

converges from behind forward between the posterior portion of the callosal band above and the optic thalamus below (see fig. 3). The greater portion of the lateral ventricular wall is there occupied by the tail of the caudate nucleus, above which the subcallosal bundle ends, while the fibres of the tapetum, which stream to or from the callosal band, curving around the tail of the caudate, overlap the ending of the subcallosal bundle. The suggestion of the continuity of the two is indeed strong. In any microscopical preparations where all the fibres are cut across and where all appear alike, it is quite impossible to recognize a line between the two. A lesion at this point would certainly involve both the fibres of the tapetum and those of the subcallosal band. Even some distance in advance of the ending of the bundle a lesion of the tract, by encroaching upon the closely adjoining fibres of the corpus callosum, might be followed by traces of degeneration in the tapetum on the one hand and in the frontal and parietal regions of the hemisphere on the other. In such a case, too, preparations containing vast numbers of fibres cut across must be misleading. In sections, however, where the thinnest bundles may be traced in their continuity, the posterior course of the subcallosal fasciculus is very plain (figs. 1, VII, and 4).

As to the nature of the tapetum, it is well to bear in mind that the last word has not yet been said on the composition of the corpus callosum. Hamilton [10] may have been wrong in his conclusions on its nature, but Beevor [3], who attempted to correct the error, was not altogether right. Cajal's silver impregnation sections are very convincing, and his [22] conclusion is that the corpus callosum is constituted in great part of collaterals of the projection and association fibres of each hemisphere. Roussy's [24] belief is "that a certain number of fibres depart from the optic thalamus and, by way of the corpus callosum, arrive at the cortex, and even in the thalamus of the opposite side." It is certain, too, that the corpus callosum contains a number of projection fibres of the ancient olfactory system. It must, therefore, be conceived as a commissural band which contains elements of many or even of all kinds of fibres of each hemisphere on their way to or from the opposite side. In the light of such a conception it will be readily understood how any portion of the corpus callosum may be present, though the rest be congenitally absent. If, therefore, any portion of the thalamic or the other fibre systems in the temporal and occipital regions attained a certain degree of development, the tapetum may very well have been present in the defective brain described by Onufrowitch and Forel.

The *Stria terminalis* or the *Stria cornea* is a prominent linear projection in the groove between the caudate nucleus and the optic thalamus. With certain differences in detail, it is the general agreement of Arnold [1], Meynert [16], Koelliker [12], Ganser [9], Edinger [6], Probst [21], Dejerine [4] and others, that in animals it is a fibre tract which begins in the masses of grey matter in the region of the anterior perforated space—the nucleus amygdalæ, the anterior portion of area pyriformis, the uncus, &c.—and which, after surrounding the optic thalamus, ends in the same masses again. Cajal [22] comments on the extreme difficulty of following this fibre band in man. His study of the tract in young mice has led him to the conclusion that the stria is both a commissural—by way of the anterior commissure—and a projection system of fibres belonging to the olfactory apparatus.

In his degeneration experiments on monkeys, dogs and cats, Probst [21] found the stria to degenerate in both directions. He could trace degeneration in front into the nucleus of Ganser, and behind into the tip of the temporal lobe.

By the method of longitudinal sectioning it has not been yet possible to establish the continuity of the fibre bundles composing the stria terminalis throughout their length in the human brain. The stria is most prominent over the superior (dorsal) part of the thalamus, in the groove between it and the caudate nucleus. In that particular situation the bundles of the frontal and parietal portions of the thalamic fan abut against the thalamus in a manner that might be very misleading in sections in which large numbers of fibres are cut across. At their junction with the thalamus the lateral portions of the stout frontal and parietal bundles pass down on the lateral surface of the lateral thalamic nucleus. There they at once break up into a matted brushwork which, in these sections, produces the very characteristic appearance of the lateral aspect of the lateral thalamic nucleus—the lamina medullaris externa. The mesial portions of the bundles in question, however, do not break up into a brushwork to the same extent. As they impinge upon the thalamus, they bend either forwards or backwards, and make a mesial bulge in the dorso-lateral groove of the thalamus, where they proceed for a considerable distance before sinking into its substance (fig. 1, VIII).

The effect produced by these frontal and parietal bundles as they impinge against the dorso-lateral edge of the thalamus is the same as when a row of camel's-hair brushes is pressed against a flat surface along its edge. Those hairs which strike the surface bend in different

directions and the hairs of adjoining brushes will become intermingled; while those situated beyond the edge will pass straight down.

It is, of course, possible that mixed in among these thalamic fibres are others which pursue an arcuate course around the thalamus. It is certain, however, that the number of such fibres, if they exist in the human brain, must be very small. A number sufficiently large to form even a thin bundle could hardly fail to be detected in longitudinal sections of flattened-out tissue. It is also certain that the main bulk of the stria terminalis in man is produced not by such arcuate fibres, but by the linear bulge of the thalamic fibre-bundles as they impinge upon the lateral edge of the thalamus.

Much longer fibres than those which constitute the stria terminalis can be observed on the surface of the thalamus close to the stria. The thin superficial covering of fibres on the dorsal, posterior and inferior surfaces of the thalamus—the stratum zonale—may be peeled off with ease from the nuclear masses within. Ranson [23] has described such a long strand of tissue which he dissected away from around the thalamus, and which he called the *Fasciculus thalamo-temporalis arcuatus*. He gives, however, no account of the miscroscopical appearance of that strand, and its differentiation from the thalamo-temporal fasciculus described by Arnold is difficult. Serial microscopical sections cut in the longitudinal course of that band made in the present study show nowhere bundles of fibres extending from one end of the long strip to the other.

The Orbital and Prefrontal Thalamic Radiation.

The course of the fibres between the orbital and prefrontal regions of the cortex and the optic thalamus is quite unlike that of the other contingents of the thalamic radiation. From the prefrontal cortex the fibres at first curve downward and backward; from the orbital area they sweep upward and backward. Upon reaching the anterior border of the caudate nucleus, both sets of fibres curve abruptly upward, in front of and parallel to the outline of the nuclear mass for a distance of about 0·5 cm. In that situation the fibres contribute to the beginning of the subcallosal bundle. They are then gathered into thick strands which pursue a long downward and backward course through the substance of the anterior portion of the caudate nucleus, the lowest of them bending over the anterior commissure (fig. 1). In their course through

the nuclear mass the bundles divide and anastomose at frequent and irregular intervals, so that this portion of the thalamic fan has the appearance of a coarse, crude network. It is important to understand, however, that this repeated division and anastomosis of the bundles takes place not only on a sagittal plane, but in a mesial direction as well. The consequence of this is that the mesially-bulging mass of the caudate nucleus above the anterior commissure is filled by these thalamic bundles. Since the fasciculi are bent in a mesial direction, a number of them are cut obliquely in sagittal sections where they branch out from their parent bundles, at the anterior and posterior borders of the head of the caudate nucleus.

Upon reaching the anterior end of the lateral portion of the thalamus, the thick bundles break up into thinner fasciculi which pursue a parallel course for some distance and then diverge. Throughout their long course these strands show no tendency to break up into a brush-work of fibres, such as is the case to a greater or less extent with the other contingents of the thalamic bundles.

It will be remembered that the anterior surface of the thalamus bears a rough resemblance to the narrower pole of an egg, in which the anterior nucleus is wedged in between the anterior portions of the converging lateral and mesial nuclei. Below, the anterior portion of the ventral nucleus is in contact with the lateral nucleus. The sagittal sections studied are those contained in the lateral portion of the thalamus for a thickness of about 5 mm. These sections, therefore, contain but a small portion of the anterior and of the ventral nucleus—their most lateral portions.

Lewandowsky's [14] researches tend to show that the anterior nucleus of the thalamus has no direct connection with the cortex. His conclusion is corroborated by the results of the present study to the extent that the thick bundles of fibres which are found in the anterior portion of the thalamus on its lateral side traverse this region without breaking up. This author is of the opinion, too, that there exists a pathway between the anterior nucleus of the thalamus and the subthalamic body. As will be presently seen, the work of other investigators in part contradicts this opinion. It has not been possible to establish in the present study whether such a pathway exists or does not exist. The longitudinal sections, however, do point to a possible source of error in this connection. As the bundles of fibres are traced in their longitudinal course downward and backward, a number of them are seen to impinge upon the capsule of the subthalamic body. Some of

these bundles become intermingled with the dense network of the capsule and are thus lost to view; others, however, penetrate the capsule and traverse the substance of the subthalamic body for some distance. In the space between the anterior portion of the thalamus and the subthalamic body these bundles diverge; they are, therefore, more and more cut up in these sections, so that upon approaching the subthalamic body their continuation is indicated by a series of short strips (fig. 1, IX). In sagittal sections the subthalamic body appears filled with a multitude of islands of transversely cut bundles. In the midst of these, the short longitudinal strips of divided orbital and prefrontal bundles become lost. Their further course was not ascertained in the present study. Since this contingent of fibres arrives at the subthalamic body by way of the anterior portion of the thalamus, some of its most mesially lying strands might easily be mistaken for a pathway connecting the two structures.

Such a connecting pathway between the subthalamic body and the anterior nucleus of the thalamus, is to a certain extent negatived by the observations of Roussy [24]. After having destroyed the greater portion of the thalamus including the anterior nucleus in a monkey, he was unable to find any trace of degeneration in the subthalamic body.

This observation of Roussy's is incompatible with the picture presented by the sections in the present study. If bundles of continuous fibres traverse both the anterior portion of the thalamus and the subthalamic body, then their destruction between those points should be followed either by direct or at least by traces of retrograde degeneration in the subthalamic body. Yet in the experiment mentioned Roussy found the latter body to be intact.

That the thalamic radiation contains both corticofugal and thalamofugal fibres, has been abundantly demonstrated by the researches of v. Monakow [17], Bechterew [2], Dejerine and Long [5], Probst [20], Roussy [24], E. Sachs [25], Fukuda [8] and a large number of other investigators. If those prefrontal and orbital bundles which traverse the subthalamic body in the human brain contain cortico-fugal fibres, then an injury to those portions of the cortex should be marked by tracts of degeneration extending into the subthalamus.

v. Monakow [17] destroyed the greater portion of the cortex in a new-born dog (Gudden's method). Six months later an examination of the brain showed the thalamus very much reduced in size on the injured side, but the subthalamic body appeared normal.

After ablation of the posterior frontal region of the dog's cortex,

Bechterew [2] found degeneration extending to the subthalamic body.

Of course, the posterior frontal region of the dog's cortex may not correspond to the prefrontal area of the human cerebrum. Yet even so, the findings in the present study are more strengthened by the positive results in Bechterew's experiment than they are weakened by the negative results in Monakow's case. The failure of development of a few strands of traversing fibres would probably cause too small a diminution in the size of the subthalamic body to be readily appreciated; while the observation of tracts of degeneration in that body after a cortical injury establishes the fact that cortical fibres either traverse or end in that body.

In the case where an old lesion involved all three frontal convolutions, Fukuda [8] found no atrophy in the subthalamic body. Whether this, too, should be discounted as a negative observation, or whether it signifies the fact that no fibres from the frontal portions of the cortex (as distinguished from the pre-frontal areas) pass into the subthalamic body, is for the present impossible to say. A concluding remark by the last mentioned author, in connection with two of his cases, throws some light on the subject. "It is not clear," he says, "where the bundles derived from the basal convolution-complex"—the prefrontal at the base, which include the orbital—"go . . . They certainly have no connection in the thalamus proper. At most they may pass to the most mesial portions, the tuber cinereum or the central grey matter of the third ventricle. . . ." This investigator, then, must have followed these bundles through the thalamus as far downward and backward as he could before he lost sight of their course.

My observations in the present study do not corroborate Roussy's [24] conclusion respecting the anterior thalamic nucleus as one of the sources of the anterior portion of thalamo-cortical fibres. Those lesions of the thalamus produced by this investigator, which involved the anterior nucleus, were large. They extended into the lateral portion of the thalamus and rather deep into its ventral and posterior portions. Fibres which may have their origin in regions behind and below the anterior nucleus would traverse it on the way to the anterior areas of the cortex. That large and numerous bundles do traverse the most lateral portion of the anterior nucleus, but which have their origin or their ending behind or below that nucleus is certain. If any of these fibres are thalamofugal, their destruction in their course through the anterior portion of the thalamus will be followed by their degeneration in a

direction toward the cortex; and the impression produced may easily be in that case that the anterior nucleus is their source of origin.

After an experimental lesion in the anterior portion of the thalamus in a monkey, E. Sachs [25] observed degenerated fibres between the anterior thalamic nucleus and the external, lateral or capsular side of the caudate nucleus. In this case, too, a possible source of error must be pointed out. The orbital and prefrontal bundles traverse the antero-lateral parts of both the thalamus and the caudate nucleus. These bundles contain a contingent of thalamofugal fibres. In a lesion of the anterior part of the thalamus, a certain number of the latter fibres must, therefore, degenerate in their course through the lateral portion of the caudate nucleus. It will be remembered that while traversing the caudate nucleus, the bundles join and divide and join again in a multitude of ways. Points of degeneration would, therefore, appear as very much scattered in this intricate network, and difficult to follow beyond it.

Tractus Subthalamicus.

A well-defined band of very fine fibres appears in these sections immediately beneath the subthalamic body (fig. 1, X). It lies embedded therefore, in the substantia nigra, at its highest and most lateral portion. In front the fibres become dispersed and lost in the caudo-putamen, immediately beneath the anterior commissure. Posteriorly its fibres are intermingled with the temporal thalamic fibres in front of the transversely cut auditory tract. In a number of the more mesial sections the band appears to embrace and to merge with the auditory bundle. The nature of this band of fibres has not been ascertained.

REFERENCES.

[1] Arnold, F. "Handbuch der Anatomie des Menschen, &c.," 1851.
[2] Bechterew, W. "Les voies de conduction du cerveau et de la moelle," 1900.
[3] Beevor, C. *Brain*, 1885-6, **8**, 377.
[4] Dejerine, J. "Anatomie des centres nerveux," Paris, 1901, **2**.
[5] Dejerine and Long. *C. R. Soc. de Biol.*, 1898, 1134.
[6] Edinger, L. "The Anatomy of the Nervous System"—English translation from 5th German edition, New York, 1900.
[7] Forel, A. "Gesammte Hirnanatomische Abhandlungen," München, 1907, 148.
[8] Fukuda, T. *Schweizer Arch. f. Neurol. u. Psych.*, 1919, **5**, 135.
[9] Ganser, S. *Morphol. Jahrb.*, 1882, **7**, 592.
[10] Hamilton, D. J. *Proceedings, Royal Soc. of London*, 1883-4, **36**, 349; *Journ. of Anat. and Physiol.*, 1884-5, **19**, 385; *Brain*, 1885-6, **8**, 145.
[11] Heinemann, O. *Arch. f. klin. Chir.*, 1916, **108**, 107.

[12] KOELLIKER, A. "Handbuch der Gewebelehre des Menschen," 1893.
[13] LANGLEY, J., and HASHIMOTO, M. *Journ. Physiol.*, 1917, **51**, 318.
[14] LEWANDOWSKY, M. "Die Functionen des zentralen Nervensystem," Jena, 1907.
[15] MCKINLEY, J. C. *Arch. of Neurol. and Psych.*, 1921, **6**, 377.
[16] MEYNERT, T. "Psychiatry"—English translation by B. Sachs, 1885.
[17] v. MONAKOW, C. *Arch. f. Psych. u. Nervenk.*, 1895, **27**, 45.
[18] MURATOFF, V. *Arch. f. Anat. u. Physiol.*, Anat. Abth., 1893, 97.
[19] ONUFROWITCH, W. *Arch. f. Psych.*, 1887, **18**, 305.
[20] PROBST, M. *Jahrb. f. Psych.*, 1903, **23**, 38.
[21] *Idem. Sitz. der Kais. Acad. der Wiss.*, Wien, **114**, 4, 3, 173.
[22] RAMON CAJAL. "Histolgie du système nerveux, &c." French transl., Paris, 1911, **2**.
[23] RANSON, S. W. *Arch. of Neurol. and Psych.*, 1921, **5**, 361.
[24] ROUSSY, G. "Thèse pour le doctorat de Méd.," Paris, 1907.
[25] SACHS, E. *Brain*, 1909-10, **32**, 95.
[26] SACHS, H. "Vorträge ueber Bau und Thätigkeit des Grosshirns, &c.," 1893.
[27] SHERREN, J. "Injuries of Nerves and their Treatment," London, 1908.
[28] WERNICKE, C. "Lehrbuch der Gehirnkrankheiten, &c." 1881.

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A NEW CONCEPTION OF THE ELEMENTS OF SENSATION.

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I.—Introduction.

We owe to Head our deliverance from the chaos which existed with regard to the afferent nervous system up to the time of the publication of his reconsideration of the distribution and function of the peripheral nerves. By means of investigations by measurable tests of each form of sensation, he was able clearly to demonstrate that what had been termed "diminished sensibility" was really a state in which some forms of sensation had been lost whilst others were retained. He was able to prove conclusively that "parts which have universally been considered to be areas of diminished sensibility turn out to be totally insensitive to certain higher forms of stimulation." In the study of the recovery of cutaneous sensation after suture of a peripheral nerve, he discovered two stages. During the earlier stage there was a gradual diminution in the area insensitive to pain produced by the prick of a pin, and to heat and cold, but the recovered sensibility was appreciably altered. The prick evoked a sensation which radiated widely and caused unnatural discomfort, and although the extremes of temperature could be appreciated no sensation of heat or cold was induced by intermediate thermal degrees. During the later or second stage of recovery the affected part began to become sensitive to light touch and

to degrees of temperature which induced sensations of "warm" and "cool." With further improvement it became possible to discriminate two points applied simultaneously, and the characteristic radiation of the first stage gradually disappeared as more accurate cutaneous localization returned.

Such observations during recovery after suture of a peripheral nerve demonstrated the existence of two systems in cutaneous sensibility, which Head named the protopathic and epicritic, and it was thought that the former system regenerated more rapidly and with greater ease than the latter. The crucial test of this division into two systems was the classical experiment upon Head's own arm. In this experiment the radial nerve was divided at its origin from the musculo-spiral, and the musculo-cutaneous nerve at the point where it perforated the deep fascia, just proximal to its division into the two branches which supply respectively the anterior and posterior aspects of the pre-axial half of the forearm. Some days later it was discovered that, in addition to the larger area in which, except for the dissociation at the edges, there was a complete loss of cutaneous sensation, there existed a small triangular portion where normal sensation to light touches with cotton wool and Von Frey's hairs was retained, but there was insensitiveness to the prick of a pin. The dissociation of the sensation of this triangle was the reverse of that found at the periphery of the larger area, where the prick of a pin was appreciated but there was no appreciation of light touches with cotton wool. The prolonged investigations of these complementary areas of dissociated sensibility established the existence of the two systems in cutaneous sensibility, and proved that these two systems were independent and did not depend upon simply a modification of the same system of nerve fibres and end organs.

To these two systems found in cutaneous sensation Head added a third, deep sensibility, which was capable of responding to pressure, passive movement of joints, and pain caused by excessive pressure. He found that a part endowed with only this third form of sensibility possessed not only the ability to recognize a pressure stimulus, but also the power to localize it with remarkable accuracy. Furthermore it was decided that "the fibres subserving this form of sensation run mainly with the motor nerves, and are not destroyed by division of all the sensory nerves to the skin." Our knowledge of deep sensibility is based almost entirely upon an investigation of the residual sensation in the experiment upon Head's own arm. The nerves divided in this

experiment were selected because it was thought that, since these nerves were usually considered as purely cutaneous in distribution, a large area of skin would be rendered completely insensitive and yet the sensibility of the subcutaneous tissues would be undisturbed. Observations will be advanced in this paper to show that it is anatomically impossible to isolate deep from cutaneous sensibility, and that, by employing methods which Head has used for the investigations of cutaneous sensation, it is possible to find after division of peripheral nerves at various levels most intricate types of dissociation in the various forms of sensibility grouped as "deep." Furthermore, having obtained an insight into the production of these dissociations, it is practicable during regeneration after suture to recognize two systems in deep sensibility.

My attention was directed to this subject during the progress of a study of the late results of secondary suture of certain peripheral nerves of the upper limb [7]—as the median and ulnar—since it became apparent that the sensory condition found did not conform with our present conception of the subject. The chief discrepancy had reference to deep sensibility, and most of the investigations recorded in this paper are concerned with this aspect of sensation. It was discovered in some patients, after suture of the median, that all the muscles—when tested individually—had recovered voluntary power and yet the hand was of slight practical service when the patient attempted purposive movements necessary on his return to work. These patients complained that they lost the grip of their tools, and on further inquiry it was found that they could use the hand fairly well as long as they concentrated upon the movements, but it failed to function satisfactorily as soon as they ceased to watch what it was doing. Several volunteered the information that the hand was useless in the dark or when they were unable to observe what they were trying to do with it. Such complaints were made by patients some three or more years after the performance of end to end suture, even when the cutaneous sensation had made a fair recovery and all the muscles, when tested individually, exhibited good voluntary power. It seemed clear that such a disability could only be due to a loss of afferent stimuli from joints, muscles, tendons and other deep structures. It was only practicable to investigate directly the extent of the recovery of fibres conveying sensory impressions from such deep structures as the joints. An investigation as to the sense of posture and the appreciation of passive movements in the finger and thumb articulations supplied by the nerve was carried

out and it was discovered that these were generally lost, or at the best very defective, even when fully three years had elapsed since the time of the suture. This loss of appreciation, or defective recognition, of passive movement in the joints supplied by the nerves was found irrespective of the level of the suture; although, according to Head, there would be no serious loss of deep sensibility after section of the median or ulnar nerves low down, e.g., at the wrist. This inquiry into the recovery after end to end suture of afferent fibres from joints gradually directed me to the investigations recorded in this paper.

II.—The Anatomy of Deep Sensibility.

By the subdivision of sensation into cutaneous (epicritic and protopathic) and deep, we are at once confronted with certain anatomical difficulties, which are emphasized in the hand and digits where much of the experimental work upon sensation has been performed. We cannot separate anatomically the fibres distributed to cutaneous and subcutaneous structures of any sensory nerve of sufficient size to warrant its use as a source of information about sensation. No nerve trunk or branch, of sufficient size to receive a name, has an exclusively cutaneous distribution. My own clinical investigations prove that the radial [8] besides supplying skin is distributed to certain articular structures, and careful dissection of nerves which have unfortunately been described as "purely cutaneous" will show that a large proportion of fibres terminate in the subcutaneous tissues. Of course such a gross method of investigation as dissection does not give us any information about the function of these fibres which can be traced into deeper structures, but in view of the clinical findings after division of the radial nerve (which is usually designated a purely cutaneous nerve), we must not assume that any nerve, of sufficient size to justify its selection for experimental work upon sensation, is purely cutaneous until it has been proved. In the course of this work the extreme difficulty of determining clinically whether the sensory fibres of a nerve are distributed solely to skin or not has become manifest, the chief hindrance arising from the fact that we cannot ascertain for certain whether some aspects of sensation are subserved by fibres terminating in skin, or subcutaneous tissues, or both. This difficulty is well illustrated by localization. From the experiments upon localization it is clear that fibres subserving this form of sensibility terminate cutaneously and subcutaneously. It seems possible from my own observations and those of others that discrimination may be also served by both cutaneous and subcutaneous systems,

but there are even greater technical difficulties to be overcome in making a decision with regard to this form of sensation. At first sight the experiment upon Head's own arm seems to establish discrimination as purely dependent upon a cutaneous supply, but it depends upon the *assumption* that the radial and the terminal branches of the musculo-cutaneous are purely cutaneous nerves, and since in a larger proportion I have found this not to be the case, the results cannot be accepted as proof that discrimination is only a cutaneous form of sensation. In the case of division of the median and ulnar it is clearly quite impossible to advance any proof with regard to this question owing to the complex anatomical distribution to subcutaneous tissues in this region. Whereas we know accurately the normal cutaneous distribution of the median and certain variations [6] in its cutaneous supply, we find that the corresponding deeper tissues receive sensory fibres from at least three sources. The subcutaneous structures of the palmar surface of the thumb, index and middle fingers are supplied from the median nerve direct by means of the digital branches, and from branches arising from the main trunk proximal to the wrist which probably run chiefly with the muscular branches, and so pass to their distribution along tendons. The subcutaneous tissues of the palm corresponding to the cutaneous distribution of the median are supplied, first by branches from the nerve itself as it breaks up in the palm, secondly by branches which pass down with the long tendons, and thirdly from the deep branch of the ulnar or perforating branches of the radial or both. The latter two possible sources of sensory fibres are shown by the fact that even after division of the median nerve in the upper arm, pressure and often pressure-pain can be recognized over the whole of the palm in some patients, and in all over a considerable part of the palm; and similarly after division of both the median and the ulnar in the arm contact and pressure pain are appreciated over part of the palm, especially on the outer side.

The distribution to subcutaneous tissues in the case of the ulnar is not quite so complex, but sufficiently intricate to make it impracticable to isolate it from the cutaneous supply. In the hand deep sensibility is only in part subserved by fibres which run with muscular branches, since the digital nerves—which are generally regarded as cutaneous—definitely supply the articulations [8]. One form of sensation included under the term of deep sensibility is therefore invariably affected by division of the median or ulnar, whether the section of the nerve occurs at the wrist or in a more proximal part of the limb.

The complex anatomical arrangement of the sensory supply to the subcutaneous tissues of the hand makes it exceedingly difficult to investigate what has been termed deep sensibility; it is not accurate to regard it as the residual sensation after division of a purely cutaneous nerve unless we are certain that a nerve so designated has solely a sensory distribution to skin, and from the results recorded in this paper I maintain that we cannot so adjudge the radial nerve. Most anatomical text-books describe the radial as "purely" or "solely" cutaneous, but it seems evident that in the past anatomists have designated nerves as purely cutaneous on insufficient evidence. This appears to have misled Head and his co-workers into the belief that in "a human experiment in nerve division" only cutaneous sensation was destroyed, and deep sensibility persisted undisturbed.

From these conclusions it would appear that any division of sensation into cutaneous and deep must be regarded as artificial, and is apt to be misleading when applied to clinical work owing to the complex anatomical distribution of sensory fibres to the subcutaneous tissues.

III.—The Normal Anatomical Distribution of Afferent Nerves to the Interphalangeal and Metacarpo-phalangeal Joints.

After a few patients had been examined with reference to the extent of the recovery of sensory fibres supplying the articulations of the digits, a difficulty presented itself owing to our imperfect knowledge of the normal distribution of peripheral nerves to the interphalangeal and metacarpo-phalangeal joints. Consequently it became necessary to discover precisely the normal distribution of the various nerve trunks to the joints, in order to be able to estimate accurately the recovery which had occurred. The details of this part of the work have already been fully recorded in a recent paper [8] and it is necessary only to summarize the conclusions bearing upon deep sensibility.

In all fifty-one patients were examined and they were selected because it was known that a complete division of definite peripheral nerves of the upper extremity existed. Any patient manifesting such complications as division of tendons or limitation of mobility of joints was disregarded for obvious reasons.

The examination was first made on the normal side in order to make the patient quite familiar with the method and what was expected of him; secondly to provide a standard and control for comparison;

and thirdly to enable me to test the reliability and attention of the patient. It was surprising how few patients had to be discarded as unreliable when sufficient time was taken to make quite clear to them what was wanted, and enough patience was expended. A relatively large number, who were otherwise suitable, had to be omitted on account of arthritic adhesions. Each segment of the digit, above and below the joint to be examined, was grasped firmly by the lateral borders and then the joint was gradually and evenly flexed or extended. The segments of the digit must be grasped firmly, as Head [3] has pointed out, so that the additional pressure required to move the joint shall not be distinguishable and thus lead to the recognition of movement from impressions other than those arising from the articular structures. The movement of the joint must also be made as far as possible at a uniform rate and not too slowly. The patient was requested to state when he first felt any movement, and on answering was further asked at which joint it occurred, and also the apparent direction of the movement. The latter two questions were soon found to be of fundamental importance for any accurate investigation of the appreciation of passive movement in a *joint*, since it was discovered that patients were able frequently to recognize movement of a particular digit without possessing any knowledge of the joint at which it occurred or the direction in which it moved. Quite early in the investigation it became manifest that this recognition of mere movement of a finger was obviously dependent upon alteration in tension or position of the tendons (and consequent stimulation of the nerve endings in relation to them), and did not arise from any stimulation of afferent terminals in the bones, cartilage, and capsule of the joint. Several patients informed me that they felt the movement of something at the wrist and knew it was pulling on a finger, but were quite unable to discover from the sensation aroused at which joint the movement took place. Fortunately this source of fallacy was discovered at an early stage in the investigation, and errors arising from it were consequently prevented. From a review of other work on this aspect of sensation it seems possible that fallacies may have arisen in the past from this cause.

Another source of possible error, which was soon determined, arose from the difficulty patients had in expressing the joint at which the movement was experienced. Such a term as "first joint" was apt to be misleading, since some referred this to the metacarpo-phalangeal articulation, and others to the distal interphalangeal. Consequently it was found necessary at the outset of each examination to have a clear

TABLE I.—To show the Normal Variation in the Distribution of Afferent Nerves to the Interphalangeal and Metacarpo-phalangeal Joints.

Thumb		Index			Medius			Ring			Little		
Interphal.	Met.-phal.	Distal interphal.	Prox. interphal.	Met.-phal.	Distal interphal.	Prox. interphal.	Met.-phal.	Distal interphal.	Prox. interphal.	Met.-phal.	Distal interphal.	Prox. interphal.	Met.-phal.
(1) Median chiefly Radial supplementary	(1) Radial chiefly Median supplementary	Median	Median	(1) Median chiefly Radial supplementary	Median	Median	(1) Median chiefly Radial supplementary	(1) Ulnar	(1) Ulnar	(1) Ulnar	Ulnar	Ulnar	Ulnar
(2) Median alone 42 per cent.	(2) Radial alone 15 per cent.	(invariably)		(2) Median alone 25 per cent.	(invariably)		(2) Median alone 42 per cent.	(Probably supplemented by median)		(2) Ulnar alone 5 per cent.	(invariably)		
	(3) Median alone 16 per cent.			(3) Radial alone 8 per cent.			(3) Radial alone 8 per cent.	(2) Ulnar alone 25 per cent.	(2) Ulnar alone 25 per cent.	(3) Very rarely branches from radial			
				(4) Very rarely some branches from ulnar			(4) Rarely some branches from ulnar						

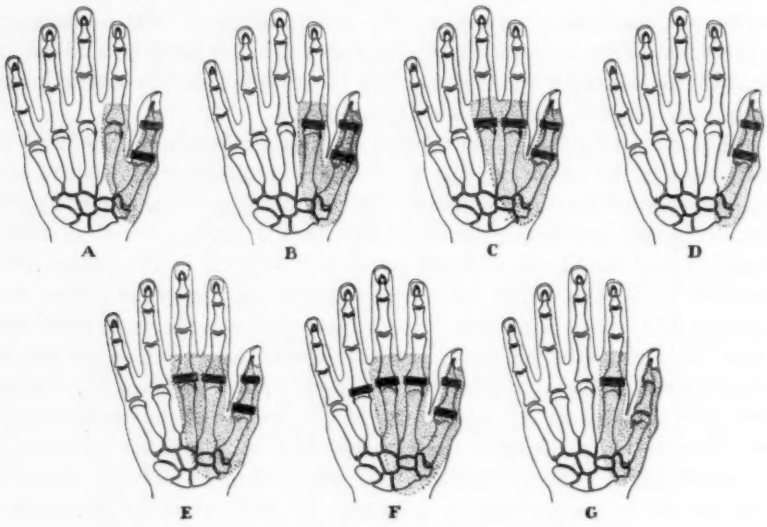
understanding with the patient as to the terminology he adopted for the various joints. The results of this anatomical inquiry into the normal supply of the afferent fibres to the interphalangeal and metacarpo-phalangeal joints are summarized in Table I, but it must be understood that the percentages there stated can be regarded as only approximate, since only fifty-one patients were examined.

The most surprising result found in these examinations was that no difference in the extent of the loss of the recognition of posture and appreciation of passive movement was produced by section of the nerve under inquiry at different levels in the limb, a precisely similar distribution being found whether the nerve was severed in the upper arm, forearm, or at the wrist. In seven patients (median four, ulnar two, median and ulnar one), the division was at the wrist, and there had been no division of tendons, yet the loss of appreciation of passive movement was just as widespread and as profound as when the nerves had been divided in the upper part of the forearm. In twenty others the division had occurred in the forearm, and in a number of these in its distal part. The patients in the latter category did not manifest any loss of the recognition of pressure, yet the loss of appreciation of posture was just as extensive as after section in a more proximal part of the limb, even where one or more digits were completely anæsthetic to all forms of stimulation.

It is of particular importance to notice the condition found in fourteen patients in which the musculo-spiral had been severed, since the study of these patients really resolved itself into an investigation of the distribution of the radial and lower external cutaneous branches of this nerve to the joints. In two the recognition of passive movements appeared to be perfect in all the joints, but in the other twelve one or more articulations of the thumb or fingers were affected, and the extent of this distribution was found to be subject to considerable variation. It will be remembered that there was no disturbance of the perception of passive movement in Head's historical experiment upon which depends our present knowledge of deep sensibility; and it seems possible, from the fact that a similar result was found in only two patients out of fourteen, that this form of distribution is the exception rather than the rule. Furthermore in view of the evidence of the very frequent presence of sensory fibres in the radial for the supply of certain articulations of the digits, it is no longer possible to regard the radial as a purely cutaneous nerve.

In the course of this study a very intimate relationship between

the variations in the cutaneous (epicritic) and articular distributions of the various nerves was observed, and this is illustrated in fig. 1 :—



■ = Complete loss of appreciation of passive movement.
▬ = Impaired recognition of passive movement.
▒ = Extent of anæsthesia to lightest possible stimulations.

Type A = 1 patient.
,, B = 4 patients.
,, C = 8 patients.
,, D = 1 patient.
Type E = 1 patient.
,, F = 1 patient.
,, G = 1 patient.

FIG. 1.—To show the intimate relationship between the cutaneous (epicritic) and articular distributions of the radial nerve.

The loss of the appreciation of passive movement in the joints of the digits which exhibit no anæsthesia to tactile pressure is at first sight rather mystifying in view of our present conception of the pathway for the deep afferent impressions, i.e., along nerve-fibres which run chiefly with muscular branches and so reach the articulations by the way of such channels as tendons and blood-vessels. This view must largely disregard the digital branches of such nerves as the median and ulnar as a source of articular branches to the interphalangeal and metacarpo-phalangeal joints, and yet a simple dissection of these branches will demonstrate clearly fine filaments which pass to the periosteum of the phalanges and to the interphalangeal articulations. It may be presumed that these branches from the digital nerves are either afferent or vasomotor in function. The results found in the

clinical examinations just recorded of patients suffering from division of the median or ulnar at the wrist, uncomplicated by any injury to the tendons, appear to show conclusively that some of these filaments are afferent in function and transmit information which enables us to appreciate the site, direction, and range of passive movement. Since the extent of the loss of appreciation of passive movement was not altered by the anatomical level of the section of the nerve, it appears that few, if any, fibres subserving this form of deep sensibility run with the branches to forearm muscles, the tendons of which are inserted into the phalanges. Several patients suffering from division of the median or ulnar at the wrist were able to recognize "movement" of a particular finger, probably as a result of alteration of tension or position of the long tendons; but it was clear that this knowledge was not produced by stimulation of afferent terminals in the neighbourhood of the joint, since some of them explained that they felt "the pull at the wrist," and so "guessed a finger was being moved." None of these were able to recognize at which joint the movement occurred, or in what direction it was made.

These conclusions have been verified upon a number of patients examined three or more years after suture of the median or ulnar nerve at the wrist, who at the best still exhibited very defective recovery of the appreciation of passive movement in the joints supplied by the affected nerve. From these investigations it appears that the digital nerves are the only important source to the joints of branches which transmit impulses that enable us to recognize position and movement.

On applying this knowledge to the examination of large numbers of patients upon whom end to end suture of the median, ulnar, or musculo-spiral nerves had been performed, it was found that this form of sensation, irrespective of the level of the suture, failed to show any signs of recovery until a very late stage—a time when there was evidence of return of epicritic sensibility.

IV.—Localization.

The findings with regard to spacial recognition in three dimensions led me to investigate other aspects of deep sensibility.

At present it is believed that pressure is localized with remarkable accuracy even when there is a complete loss of cutaneous sensibility, and it is surmised that this form of sensation is dependent upon

afferent fibres which run in muscular, articular, and subcutaneous branches.

Hitherto, no perfectly satisfactory method for testing accurately tactile localization has been evolved. Most methods now in use only demonstrate very gross defects, and fail to furnish measurable results. The tests most frequently adopted in the investigation of tactile localization only show such a gross error as failure to recognize correctly the segment of the digit upon which the pressure has been applied—a defect which I have found to occur several times in apparently normal individuals [9]. Consequently an effort was made to discover some method which would supply more accurate information about the power of localization, and also provide measurable results. The method found to be most serviceable and practicable was a slight modification of that described as Henri's, but, unfortunately, it has not been possible for me to procure the original description of his method. The patient, having the part to be tested obscured from his vision, marked upon a life-sized diagram the position of the point judged to be stimulated, whilst the observer recorded on another similar diagram the exact point touched. After a sufficient number of points had been localized, the two diagrams were superimposed and the two points recorded in each test were marked on one diagram—in different colours or by distinctive signs, and then the error in each case was measured off with a millimetre scale. From these measurements, if a sufficient number of points had been localized, the average error for the whole or individual parts—as each digit—could be determined. In the latter part of the investigation only one chart was used, the observer recording the exact point stimulated after the person examined had marked the point where he felt the stimulation; and this simpler procedure proved as successful, and apparently as reliable, as the more tedious original form.

Using this method, which possesses the great advantage of giving measurable results, the following experiments were performed:—

Experiment 1.—This series, in which ten members of the medical profession provided the subjects for examination, was undertaken at the outset for two principal reasons. In the first place it was thought that any possible fallacy due to unfamiliarity with the diagrams would be reduced to a minimum; and, secondly, such a series would provide valuable information with regard to the introspective aspect of this form of sensation. The tactile pressure was made by a blunt instrument about 0·2 cm. in diameter. The palmar and dorsal surfaces of

each hand and digit were explored in turn. Twelve stimulations were made on each surface, eight or nine of which were on the digits and the rest on the palm or dorsum of the hand. The average error for the ten subjects was found to be 0·6 cm. for the palmar and 0·5 cm. for the dorsal surfaces of the right hand and fingers, and 0·5 cm. for both surfaces of the left hand and fingers.

Experiment 2.—In this series, ten non-medical people were examined and only the palmar surface of the two hands and digits explored. The ten were composed of clerks, departmental stewards, porters, and second-year students. The same number of stimulations were made, and the same proportion on the hand and digits, by the same instrument as in the previous experiment. The average error for the ten was 0·6 cm. for the right hand and 0·7 cm. for the left. The close similarity in the results in the two experiments is rather remarkable, and shows that any error due to unfamiliarity with the charts, at any rate for the palmar surface of the hand and digits, must be very slight. This conclusion was confirmed by a large series of tests carried out upon pensioners under my charge, in whom an average error of 0·6 cm. was found for the palmar surface of the hand and digits on both sides.

Experiment 3.—This series was undertaken to discover the normal average error for the individual fingers and to find out if there was normally any definite variation in the power of localization in the different fingers. Two people were chosen from each of the former experiments and twelve pressure stimulations (six on the palmar and six on the dorsal surface) were made on each finger of right hand. As far as possible two stimulations were made on both surfaces of each segment of a finger.

The average error for the four persons examined was found to be 0·4 cm. for the index, middle, and ring fingers, and 0·3 cm. for the little finger; from which it appeared that the power of localization did not vary to any obvious extent in the four fingers.

Further details and tables showing individual errors in these three experiments are given in the paper previously referred to.

Experiment 4.—From the results which were being found on applying this test to patients suffering from division of peripheral nerves, it was decided to perform a series of tests using as a stimulus a hair, which could not possibly stimulate any but cutaneous nerve terminals. For this investigation three medical people were chosen from those used in Experiment 1 and a similar number from the non-medical group of

Experiment 2. The same number of stimulations were made with the hair as in the former experiments where pressure had been used as the stimulus, and the conditions under which the tests were performed were identical with those of the previous experiments. It was found that a purely cutaneous stimulus could be localized very accurately; in Table II the results are compared when using a hair and when using pressure with an instrument 0·2 cm. in diameter. The latter records had been taken some weeks previously.

TABLE II.

	Right Hand		Left Hand	
	Hair	Pressure	Hair	Pressure
SL.	·5 cm.	·4 cm. ..	·7 cm.	·6 cm.
SJ.	·5 ,,	·7 ,, ..	·7 ,,	·5 ,,
EAL.	·6 ,,	1·0 ,, ..	·5 ,,	·8 ,,
AFCD.	·5 ,,	·5 ,, ..	·4 ,,	·6 ,,
AG.	·6 ,,	·7 ,, ..	·7 ,,	·7 ,,
RF.	·5 ,,	·5 ,, ..	·5 ,,	·5 ,,
Average	·5 ,,	·6 ,, ..	·6 ,,	·6 ,,

From these results it will be seen that accuracy of localization is practically the same, for either a purely cutaneous stimulus or pressure, in individuals with normal sensation.

It is of interest to notice that in the observations made upon Head's hand [5], it was found that accurate localization of cutaneous stimuli did not return until the skin was sensitive to tactile hairs after shaving.

Experiment 5.—After the former more or less preliminary experiments, which were undertaken chiefly to gain experience and establish the normal degree of error in localization, had been carried out, the pressure test was applied to twenty patients who were known from surgical observations to have suffered from division of one or two peripheral nerves of the upper limb at various levels. A similar number of stimulations as in Experiments 1 and 2 were made over the region of the cutaneous distribution of the affected nerve and, for comparison, on the normal part of the same hand or a similar region on the unaffected hand. Stimulations were made with the same instrument as that used in the other experiments. In ten patients, the observations were taken shortly after the performance of secondary suture of the injured nerve, at a time too early for any regeneration to have occurred. The results are tabulated in Table III.

The average error for the ten patients over the cutaneous field of the sutured nerve was 1·4 cm., whereas on the normal part it was 0·6 cm.

TABLE III.—LOCALIZATION (PRESSURE) TESTS, AFTER COMPLETE NERVE DIVISION AND SUTURE AT A TIME WHEN NO REGENERATION HAD OCCURRED.

Patient	Nerve	Site of suture	Average error for localization over area of epicritic loss	Average error for localization over normal area
T. E.	Median	Upper forearm	1·2	·6
J. D.	Median	Middle of forearm	1·4	·5
H. S.	Musculo-spiral	Elbow	1·1	·4
T. M.	Ulnar	Middle of forearm	1·7	·7
A. M.	Median	Middle of forearm	1·0	·5
N. D.	Ulnar	Middle of forearm	1·2	·4
J. J. T.	Median	Arm	1·8	·6
A. L. B.	Ulnar	Elbow	1·1	·6
J. T. S.	Ulnar	Lower forearm	1·9	·8
F. S.	Ulnar	Middle of forearm	1·2	·8

In the case of T.M. two stimulations on the little finger had to be left out of the calculations since he said he was unable to place them; he knew one was "somewhere" on the little finger, but the other seemed "somewhere" on the inner part of the hand.

In seven other patients the investigation of localization was made after protopathic sensibility had made a complete recovery, but before there was any reduction in the loss of epicritic sensibility. The results of this set are recorded in Table IV.

TABLE IV.—LOCALIZATION (PRESSURE) TEST, AFTER COMPLETE NERVE DIVISION AND SUTURE, WITH RECOVERY OF PROTOPATHIC SENSIBILITY AT TIME OF OBSERVATION.

Patient	Nerve	Site of suture	Average error for localization over area of epicritic loss	Average error for localization over normal area
B. K.	Median and ulnar	Wrist	1·4	·9
A. N. K.	Ulnar	Elbow	1·4	·5
S. O.	Ulnar	Middle of forearm	1·4	·5
J. R. M.	Ulnar	Upper forearm	1·6	·5
O. R.	Median	Middle of forearm	1·4	·8
V. P.	Ulnar	Lower forearm	3·0	·5
T. T. P.	Median	Lower forearm	1·1	·5

The average error for the seven patients over the area of epicritic loss was 1·6 cm. and over the normal part 0·6 cm. This series shows that the error in localization is not diminished during the recovery of protopathic sensibility. In two additional patients considerable time had elapsed since the performance of the suture and some recovery of epicritic sensibility had occurred, as well as the return of protopathic sensibility. In both patients gross errors were found with the compass test over the cutaneous distribution of the nerve, although this was sensitive to the lightest application of a camel hair-brush. The findings of these two patients are shown in Table V.

It is of great interest to notice that in both patients the remaining

deficiency in sensation affected discrimination, localization, and the recognition of posture and passive movement in the joints supplied by the nerve.

TABLE V.—LOCALIZATION (PRESSURE) TEST, AFTER COMPLETE NERVE DIVISION AND SUTURE, WITH RECOVERY OF PROTOPATHIC AND PARTIAL RECOVERY OF EPICRITIC SENSIBILITY AT TIME OF OBSERVATION.

Patient	Nerve	Site of suture	Average error for localization over area of partial epicritic loss	Average error for localization over normal area
W. H.	Ulnar	Arm	1·0	·7
T. N. W.	Median	Upper forearm	1·3	·9

In one other patient the only evidence of any regeneration of afferent fibres was a slight recession of protopathic loss, although four years had elapsed since the time of the secondary suture of the median, and the error in localization for the anæsthetic area was 1·2 cm., whereas for the normal part it was 0·4 cm.

By the application of this method of testing localization, which gives measurable results, to patients known to be suffering from division of peripheral nerves, it is shown that, contrary to the present view, accurate tactile localization is not present even when the pressure is sufficient to stimulate the deep afferent system. It is difficult to decide whether the defective power of localization in these twenty patients was due to loss of cutaneous or subcutaneous nerve terminals, or both, since pressure may stimulate both, and although in eighteen of the patients the skin was anæsthetic, we have no accurate anatomical or physiological information about the fibres of the median or ulnar distributed to subcutaneous tissues.

Experiment 6.—Head [5] has stated that "localization is in all probability the sum of two sets of sensation, one of which arises from deep, the other from cutaneous stimulation." The foregoing experiments are in perfect agreement with this contention, but it is difficult to decide whether the errors in localization in Experiment 5 were due to the loss of cutaneous sensation only, or to a disturbance of the deep system in addition. The power of localization which remains, in the patients used in Experiment 5, must be entirely dependent upon the deep system, but for the anatomical reasons stated in an earlier section, we cannot claim that it represents the normal power of localization served by fibres terminating in subcutaneous tissues. In an endeavour to arrive more closely at a correct conception of the part played by the cutaneous and deep systems, several preparations were applied to the unbroken skin in an attempt to obtain an uncomplicated cutaneous

anæsthesia. None of these gave a satisfactory anæsthesia, until on the suggestion of my colleague, Professor R. B. Wild, a 10 per cent. solution of cocaine hydrochloride in chloroform was used. With this it was generally found practicable to get an almost complete cutaneous anæsthesia of a small area in about ten to fifteen minutes. The solution was applied to the dorsum of the left index finger in three of the subjects used in Experiment 3. When the skin was found, by testing with a wisp of cotton wool, to be satisfactorily anæsthetized the examination of localization was made by eight pressure stimulations. At a later date the normal power of localization of the same part was tested by eight pressure stimulations. The average error for the eight stimulations, in the three subjects with and without cutaneous anæsthesia, are shown in Table VI.

TABLE VI.

	Normal average error	Average error with cutaneous anæsthesia
S. L. ..	·3 cm. ..	·4 cm.
A. F. C. D. ..	·2 ,, ..	·2 ,,
S. J. ..	·2 ,, ..	·3 ,,

It will be seen that in the three subjects the power of localization was almost as accurate when there was cutaneous anæsthesia as normally. It is only possible to anæsthetize satisfactorily a small cutaneous area and this may be raised as a criticism, but although only the dorsum of one finger was examined the result of the experiment strongly favours the presumptions that :—

(1) Accurate localization is possible through the deep system alone.

(2) Since the errors in localization in the twenty patients examined in Experiment 5 were gross, there was a disturbance of localization through the deep system and the errors were not dependent upon a loss of cutaneous localization.

In several of the patients examined in Experiment 5 the division of the nerve occurred at the wrist or in the lower part of the forearm, and there was an average error of twice the normal. Therefore we may suggest with some confidence that accurate localization through the deep system alone is disturbed by a section of the median or ulnar at the wrist.

V.—PRESSURE PAIN.

To investigate deep sensibility further it was necessary to test that form of sensation which is now well known as pressure pain.

For this purpose an algometer was made for me similar to that used

by Rivers [3]. From some preliminary tests with the instrument it became clear that certain technical difficulties in its use were to be overcome, and it appeared necessary to carry out at the outset some experiments upon normal individuals in order to establish a standard procedure when using the instrument upon patients.

Experiment 1.—These preliminary tests were made upon six normal individuals, three on the right hand and three on the left, and in each the pressure was applied at eight selected points which are shown in fig. 2. At each point three readings were taken, and it was soon found

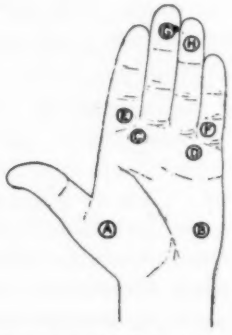


FIG. 2.—To show the position of the eight selected points used in Experiment 1 (pressure pain).

that the second and third readings ought not to be taken over the exact point of the former, since repetition of pressure over the same spot resulted in pain being experienced with much less pressure than on the previous occasion. Inequality in the three records in the same neighbourhood was found to be due to differences in the rate of application of the pressure; it was therefore necessary to apply the pressure evenly and slowly, which is by no means easy, and some of the greater differences in the three readings may be due to this cause. A third cause of difficulty was due to the personal factor, as it was not always possible to get the person examined to indicate at once the onset of the painful element in the sensation aroused by pressure. In the first series, several informed me that there was a great tendency to compare a second experience of pain with the first, which tended to disturb their judgment. These sources of fallacy make it important, as Head as already stated, to take at least three readings at each point.

The results of the investigation of the six normal individuals are given in the Table VII, which shows all the three readings at each of the eight points.

TABLE VII.—TO SHOW THE AMOUNT OF PRESSURE REQUIRED TO INDUCE PAIN, AT EIGHT SELECTED POINTS ON THE HAND AND DIGITS, IN SIX NORMAL INDIVIDUALS.

	A	B	C	D	E	F	G	H
S. J.	2·50	3·25	1·50	1·25	3·00	2·50	1·00	·75
	2·75	3·00	1·25	1·25	2·00	2·50	·75	·75
	2·50	3·50	1·25	1·50	2·50	2·50	1·25	1·00
G. M. D.	2·50	2·50	1·50	·50	2·25	2·00	·50	·25
	2·00	2·25	1·25	·50	1·00	1·50	·75	·25
	1·75	1·75	2·00	·75	1·25	1·75	·25	·25
D. S.	2·75	2·00	1·25	1·00	1·00	1·00	·25	·5
	2·00	2·50	1·00	·75	1·25	·75	·25	·75
	1·00	2·50	·75	·75	1·50	·75	·25	·25
R. F.	2·25	2·25	1·25	1·00	1·75	2·00	2·00	1·75
	2·25	1·00	1·50	1·25	1·75	1·50	2·25	·50
	1·75	1·75	1·00	1·00	1·50	1·25	1·75	1·25
L. S.	1·50	2·00	·75	1·00	1·25	·75	·50	·25
	1·75	2·00	·75	·50	1·50	1·50	·50	·25
	1·75	1·50	·75	1·00	·75	1·25	·25	·50
H. G.	2·75	3·50	1·50	2·25	2·75	2·50	2·25	2·25
	2·50	3·00	1·50	2·25	2·50	2·75	2·00	2·25
	2·75	3·25	2·25	2·75	2·75	2·75	2·00	2·25

The results of this experiment brought out the following information:—

(1) Greater pressure was usually required to produce pain in the thenar and hypothenar regions than at the other points tested.

(2) Less pressure was required at the base of the clefts between the fingers than over the palmar surface of the proximal segment of the digits. This is presumably due to the exposed position of the digital nerves as they divide in the region of the clefts into branches for the adjacent sides of the neighbouring fingers.

(3) With a single exception, less pressure was needed to induce pain over the palmar surface of the distal segment of a digit than over its proximal segment.

Experiment 2.—With the knowledge and experience gained from this preliminary investigation of pressure pain, the test was applied to a number of patients suffering from division of the median or ulnar nerves. To simplify the presentation of the results of this experiment only the average of the three readings at each point is recorded, and for ease of comparison the results of five typical tests are represented in a diagrammatic form (figs. 3, 4 and 5). As in the former experiment the pressure required to induce pain is recorded in kilogrammes.

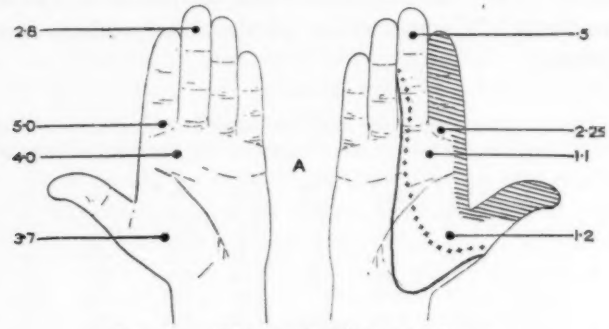


FIG. 3, A.—Division of median nerve in arm.

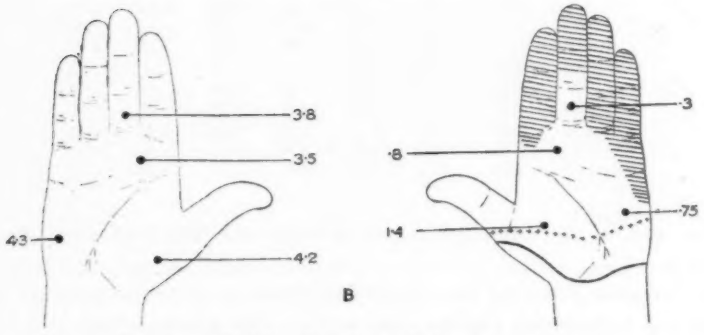


FIG. 3, B.—Division of median and ulnar nerves in arm.

Crosses = analgesia to prick of pin.
Thick line = anæsthesia to lightest applications of fine brush.
Shading = complete sensory loss.

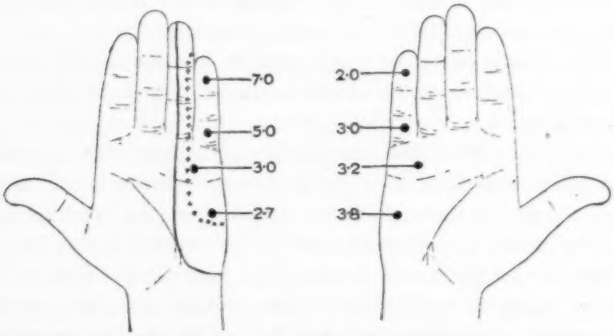


FIG. 4.—Division of ulnar nerve in upper forearm.

Crosses = analgesia to prick of pin.
Thick line = anæsthesia to lightest applications of fine brush.

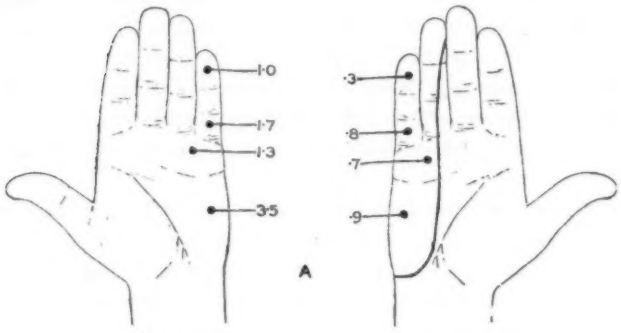


FIG. 5, A.—Division of ulnar nerve in lower forearm.
Thick line indicates anæsthesia to lightest applications of fine brush.

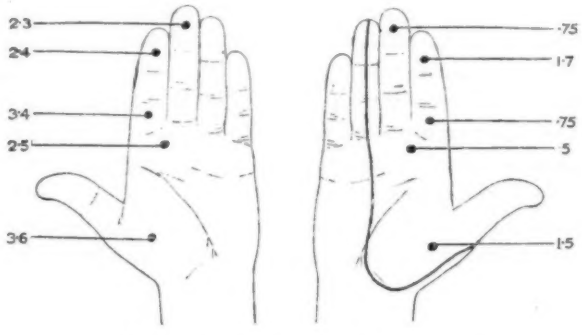


FIG. 5, B.—Division of median nerve in arm.
Thick line indicates anæsthesia to lightest applications of fine brush.

By these experiments it was found :—

(1) That it was distinctly easier to test pressure pain on the abnormal than on the sound side. This was due to the fact that when testing over an area where epicritic sensibility was lost, the patients could more readily recognize the onset of the painful element since it commenced abruptly and rapidly became intensely painful. Several patients told me that they had no doubt on the affected side, whereas on the sound side they were often in difficulty as to when the pressure became actually painful. As Head found, several expressed fear at the application of pressure on the affected side, and this, together with the

experience that on this side the pain quickly became intense, may have caused in some of the tests an abnormally low reading on the affected side.

(2) In those patients where the division of the nerve was in the distal part of the limb and there was no absolute sensory loss, the readings on the affected side tended to be definitely lower than on the sound side.

(3) In some patients with division of the median in the middle of the forearm, i.e., proximal to the supply of that portion of the flexor sublimis digitorum which flexes the index finger and distal to the origin of the anterior interosseous nerve and branches for the supply of the main flexor mass, considerably more pressure was required on the index on the affected than on the sound side. These results pointed to a disturbance, but not complete loss, of this form of sensation in the index after division of the median proximal to the origin of the most distal branch to the flexor sublimis digitorum, and indicated that some fibres for this form of sensation in the index were transmitted by this muscular branch, and probably extended to the digit along the tendon. Similarly, after division of the ulnar in the upper part of the forearm, although the inner part of the flexor profundus digitorum was capable of voluntary action, higher readings were sometimes found on the little finger on the affected side than on the sound side. It is not so easy to give an anatomical reason for this occurrence, which is found only in a proportion of cases of division of the ulnar in the forearm and is nothing like so constant as the similar condition just described in the case of the median, but it may be due to the occasional appearance of an extra branch to the flexor profundus digitorum in the lower part of the forearm.

The associated demonstrable disturbance of the appreciation of contact in these cases will be referred to in the next section.

(4) In the patients examined during recovery, when there was a complete return of protopathic sensibility (fig. 5), the readings at all points on the affected side were lower than on the normal side. This was found even over digits that at the outset had exhibited an absolute sensory loss, or which originally had given a higher reading. These results indicate that the recognition of pressure pain returns at an early stage in recovery, at the same time as protopathic sensibility. It is also significant that in cases of only partial recovery of sensation pressure pain like protopathic sensibility is one of the most constant to manifest some improvement.

VI.—Recognition of the "Contact" of Tactile Pressure.

In routine examinations of patients suffering from injury to, or disease of, the peripheral nerves, this aspect of deep sensibility is usually the only one tested. Consequently if the patient appreciates everywhere the contact of some instrument, as the head of a pin, "no loss of deep sensibility" is generally recorded in the notes. It does not seem to have been realized previously that the various forms of sensation grouped together as deep sensibility may be dissociated, and this, together with the widespread belief that deep sensibility is practically entirely transmitted by afferent fibres which run with motor nerves and reach their termination by accompanying such structures as long tendons, has been responsible for the confidence with which observers have been content to investigate simply the recognition of contact as the standard test for deep sensibility.

As is to be expected this form of deep sensibility is only appreciably affected in lesions in the proximal part of the limb, i.e., above the origin of the supply of branches to the long flexors of the digits. There is no doubt that mere recognition of contact is chiefly transmitted by afferent fibres which run in the branches to the long flexor muscles of the digits. In this respect it is instructive to refer to the fairly constant occurrence of complete anæsthesia of the distal part, and sometimes the whole of the palmar surface of the index finger after complete division of the median in the middle third of the forearm, although the division occurs distal to the origin of the main branches supplying the flexor sublimis digitorum and the anterior interosseous nerve. This is apparently due to the origin from the median trunk in the lower third of the forearm of a branch which supplies that portion of the flexor sublimis digitorum which flexes the proximal interphalangeal joint of the index finger. From a study of the number of patients with division of the median in the upper part of the forearm, where the precise anatomical level with regard to the origin of branches had been defined at operation, I am inclined to the view that a greater proportion of afferent fibres pass in the branches to the flexor sublimis digitorum than to the flexor profundus digitorum.

From personal observations it seems to be almost a rule that if any power to appreciate contact is retained in a part there is always in the same region some retention of the power to recognize pressure pain, although the amount of pressure required to induce pain may be very much greater than in the same region on the sound side. This latter

point is well illustrated by the following record, which also supports the previous contention that more afferent fibres are transmitted by the tendons of the flexor sublimis digitorum than those of the flexor profundus digitorum.

Patient, J. C. Complete division of the ulnar was found in the upper part of the forearm, just distal to the origin of branches for the supply of the flexor carpi ulnaris and inner half of the flexor profundus digitorum, which muscles possessed voluntary power. The loss of epicritic and protopathic sensibility corresponded to the full typical normal distribution. It was impossible to measure the error in the localization of tactile pressure over the little finger, as the best response to any stimulation he gave was "somewhere on my little finger," and he was quite unable to attempt to chart any of the stimulations in this region, although he invariably recognized that a contact had been made, provided sufficient pressure was used. The average of the three readings with the algometer on the two sides at four points may be conveniently tabulated for comparison.

	Sound side	Affected side
Hypothenar region	3·8 ..	2·7
Between heads of 4th and 5th metacarpal bones	3·2 ..	3·0
Over proximal phalanx of little finger ..	3·0 ..	5·3
Over distal phalanx of little finger	2·0 ..	7·0

It will be noticed that in the first two regions the reading was slightly lower on the affected side, whilst in the case of the two tests on the little finger the reading was markedly higher on the affected side, being more than three times greater on the distal phalanx.

Two other patients in whom similar results were found have been encountered. I have never seen "contact" and "pressure pain" completely dissociated. On the other hand these two forms of deep sensibility may be retained in a part without any power of localization being present, as in the little finger of the patient just referred to.

After division of the ulnar nerve at any point proximal to the origin of the branches for the supply of the flexor profundus digitorum, the area in which complete anæsthesia to all stimuli is found is very constant in extent and affects the little finger and the inner border of the hypothenar region as shown in fig. 6. After division of the median above the level of the branches supplying the long flexor muscles, the area of complete anæsthesia is by no means so constant. In sixteen cases of known complete division of the median, at or proximal to the level of the elbow joint, there was complete anæsthesia only of the index and a small neighbouring portion of the palm (fig. 7, A) in six; of the index and medius and a larger portion of the palm in five

(fig. 7, B); and the index, medius and palmar surface of thumb together with a still larger extent of the palm in five (fig. 7, C). The infrequency (only five out of sixteen) of complete anæsthesia of the palmar surface of the thumb was rather surprising, but the foregoing results were confirmed by the examination of a group of patients suffering from

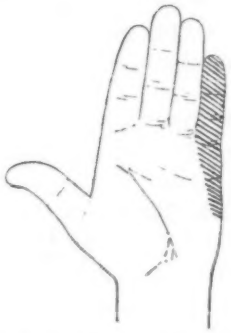


FIG. 6.—To show the typical extent of absolute sensory loss after division of the ulnar nerve in the arm.

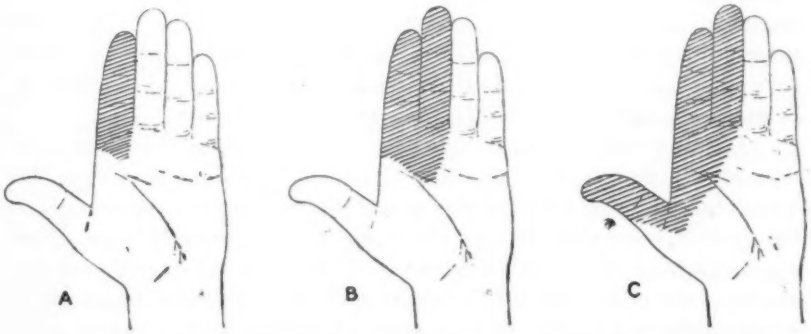


FIG. 7.—To show the variation in extent of the absolute sensory loss after division of the median nerve in the arm.

division of both the median and the ulnar nerves in the upper arm, in whom contact (if sufficient pressure was made) was recognized over the palmar surface of thumb in an even higher proportion. Consequently it must be surmised that the radial nerve, and possibly in a small number the musculo-cutaneous, by means of perforating branches, takes

part in the innervation of the deeper tissues of the palm and the palmar surface of the thumb.

VII.—Summary and Conclusions.

In each section the main conclusions which may be drawn from the experiments and investigations are presented; it now only remains necessary to restate the principal conclusions bearing upon our present conception of sensation, and these may be conveniently summarized in three divisions.

(1) It seems clear that no nerve of sufficient size to be of clinical importance, or to be selected for experimental work upon sensation, is distributed exclusively to skin. Consequently after section of any of the nerve trunks, even in the distal part of a limb, there is bound to be some disturbance of so-called deep sensibility, and it seems quite impracticable to divide sensation into superficial and deep. Besides this anatomical criticism of such a division there is to be remembered the additional confusion which may arise from the knowledge that one form of sensation at least is transmitted by both cutaneous and deep nerves. It has been proved that so-called deep sensibility is not transmitted entirely by nerve fibres which accompany muscular branches, since the sensory supply of the joints of the fingers and thumb undoubtedly arises from the digital nerves, and it seems probable that other forms of deep sensibility are in part, at least, transmitted by branches arising independently from the main nerve.

(2) The various forms of sensation included under the division of deep sensibility may be dissociated. After division of the median at the wrist there is found a loss of the recognition of passive movements at the metacarpo-phalangeal and interphalangeal joints of the digits supplied by the nerve: some power of localization is retained over the region of the cutaneous distribution of the nerve, although by means of a measurable test a gross error is seen on comparing the results with those obtained on the normal part; the least pressure is readily recognized everywhere, and the readings with an algometer show that rather less pressure is required to induce pain on the affected than on the sound side. If division of the median occurs proximal to the supply of the outer part of the flexor sublimis digitorum in the lower third of the forearm, in addition to the defects just recorded there is usually a complete sensory loss to all forms of stimulation over the distal two segments, or the whole of the index finger. In a small

proportion after section of the median at this level the loss of sensation in the index finger is less profound. Although in these there is no power to localize, the contact of pressure can be recognized and pain can be induced by excessive pressure, but on investigating the two latter forms of sensation more fully it is discovered that more pressure is required to induce the sensation of contact over the index than the medius and the reading with the algometer is considerably higher than on the sound index. The condition of what we know as deep sensibility in the index is, in such cases, in a most interesting stage and may be summarized as follows :—

(i) Loss of sense of position and recognition of passive movement in all joints of this finger.

(ii) Absolute loss of localization.

(iii) Retention of recognition of contact and pressure pain, but on the application of measurable tests it is found that these forms of sensation are grossly affected.

Little reference need be made to the effect upon deep sensibility of a lesion at a higher level, in the region of the elbow or in the arm, since, except with regard to localization which has already been fully discussed, the condition is well known ; reference is only necessary to the fact that the extent of the absolute sensory loss to all stimuli is variable.

(3) Observations upon the recovery of deep sensibility demonstrate several striking and significant features. Reappearance of the recognition of contact and appreciation of pain on the application of excessive pressure occurs early, as a rule during the stage of protopathic recovery. At first considerable pressure is required before it is appreciated, but the recovery of contact without concomitant recovery of pressure pain has never been encountered, although the extremely high reading with the algometer in two patients examined suggest that this is possible, and there does not appear to be any obvious reason why these two forms should not be dissociated. As regeneration proceeds less pressure is found to be required at subsequent examinations. As the recognition of contact and pressure pain improve there is usually a return of some power of localization, but it is very grossly defective, the error being much greater in regions where there has previously been an absolute sensory loss than elsewhere. Further improvement in localization and signs of recognition of passive movement of joints occurs very late, and not until there is evidence of recovery of epicritic sensibility. Most of my studies have

been upon patients who have had a secondary suture of the median or ulnar nerve, and under these circumstances any recovery of accurate localization or recognition of passive movements of joints is at the best very defective and frequently remains absent. After primary suture there is a better opportunity for studying the later phases of recovery. It seems very significant that recovery of recognition of contact and appreciation of pressure pain, followed often by a gross and defective return of the power of localization, occur early during the stage of reappearanee of protopathic sensibility, whilst accurate localization and recognition of passive movement only appear late, at a time when there is also evidence of epicritic return as tested by graduated hairs and the compass. That is to say the three forms of sensation concerned with spacial recognition—accurate localization, discrimination and recognition of passive movement—only recover at a very late stage, and even after primary suture are apt to remain defective.

These observations upon the recovery of certain forms of sensation after suture of a peripheral nerve suggest two important facts.

(*a*) What we have regarded as deep sensibility ought to have been subdivided, just as cutaneous sensation has been divided, into epicritic and protopathic. There is no doubt that the two forms of sensation, recognition of the contact of pressure and appreciation of passive movement, must be subserved by nerve fibres terminating in the deep tissues; the former of these returns early at a time when protopathic sensibility is recovering, whilst the latter returns at a late stage, if at all, during the time of epicritic recovery. The mere recognition of the contact of pressure is a crude form of sensation compared with the more highly graded appreciation of the direction, localization and range of passive movement of a joint.

(*b*) In the light of Head's recent work upon the sensory cortex [2], these results suggest that at the periphery, both in cutaneous and deep tissues, we have cortical and thalamic aspects of sensation. The dissociation which is encountered after the division of any large nerve trunk makes it exceedingly difficult to unravel the fundamental principles upon which sensation at the periphery is based, but when we get an accurate conception of the anatomical distribution, and in the light of this knowledge analyse the results of careful clinical examinations of a number of patients suffering from division of a peripheral nerve, the curious forms of dissociation become more intelligible. Continued examinations of the same patients during recovery seem to bring us

still nearer to a knowledge of the true state of affairs. It has just been stated that certain forms of deep sensibility constantly recover during the early stage when the area of protopathic loss is found to be receding, whilst other forms do not show any recovery until a late stage when there is clinical evidence of a return of epicritic sensibility. In the examinations of a very large number of patients I have found this to be an invariable rule.

It appears to have been generally believed that the earlier return of protopathic sensibility is dependent upon a more rapid rate of regeneration in protopathic than epicritic fibres. Such an explanation supposes some structural difference in the two systems, and Ranson [4], on histological and experimental evidence, made the suggestion that impulses giving rise to pain travel in non-medullated fibres; but more recent work by Adrian [1] shows that it is highly improbable that there is any definite structural difference in the fibres concerned with protopathic and epicritic sensation. A simpler explanation is suggested when we take into consideration all the forms of sensation which return during the later stage of recovery. The forms appearing late, which more frequently show imperfect recovery, or in quite a proportion of cases of secondary suture fail to recover, are those which Head has proved to have cortical representation; whilst the forms which exhibit early and more constant recovery are those which may be expected to persist after destruction of the sensory cortex. Therefore it seems more reasonable to expect to find an explanation of the two stages of recovery in the central nervous system, rather than to find it due to a different rate of regeneration of two sets of fibres which anatomically appear to be identical. After suture and regeneration of a peripheral nerve a much longer period may be expected to elapse before the fibres subserving cortical forms of sensation function correctly, than in the case of the fibres conducting the thalamic aspects of sensation; since a very much more complex readjustment and re-education must occur after regeneration of the fibres in the former case than in the latter. Furthermore, on the hypothesis suggested in this paragraph, we seem to have ample reasons for the more constant and perfect recovery of such aspects of sensation, as cutaneous pain, pressure pain and appreciation of extremes of temperature, than for the higher forms, as those concerned with spacial recognition.

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REFERENCES.

[1] Adrian, E. D. "The Response of Human Sensory Nerves to Currents of Short Duration," *Journ. Physiology*, 1919-20, **53**, 70.
[2] Head, H. "Sensation and the Cerebral Cortex," *Brain*, 1918, **41**, 57.
[3] *Idem.* "Studies in Neurology," vol. i, Part I, London, 1920.
[4] Ranson, S. W. "Unmyelinated Nerve-fibres as Conductors of Protopathic Sensation," *Brain*, 1915, **38**, 381.
[5] Rivers, W. H. R., and Head, H. "A Human Experiment in Nerve Division," *Brain*, 1908, **31**, 323.
[6] Stopford, J. S. B. "The Variations in Distribution of the Cutaneous Nerves of the Hands and Digits," *Journ. Anat.*, 1918, **53**, 14.
[7] *Idem.* "The Results of Secondary Suture of Peripheral Nerves," *Brain*, 1920, **43**, 1.
[8] *Idem.* "The Nerve Supply of the Interphalangeal and Metacarpo-phalangeal Joints," *Journ. Anat.*, 1921, **56**, 1.
[9] *Idem.* "Tactile Localization," *Journ. Anat.*, 1921, **55**, 249.

TOXIC POLYNEURITIS.[1]

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RECOGNITION of multiple or peripheral neuritis as a clinical and pathological entity dates from the publications of Duménil in 1864 [10] and especially of Leyden in 1880 [24]. Since that time a host of observers have studied the disease, so that the varieties of the commoner forms, the alcoholic, lead, arsenical and diphtheritic paralyses, are well known. It is not my intention to dwell on those forms the etiology of which is clear and unmistakable, but rather on the numerous lesser known types, the origin of many of which is quite obscure.

Multiple neuritis in our present state of knowledge is best classified on an etiological basis, rather than on pathological distinctions or clinical differences, and four main groups may be separated:—

(1) Those dependent on the absorption of poisons introduced into the body.

(2) Those due to autotoxæmia, or to poisons developed primarily within the body.

(3) Those due to infections of an organismal nature.

(4) Those occurring in cachectic states.

The first group may usefully be divided into two sub-groups, those due to metallic poisoning, and those due to poisoning by various carbon compounds.

The term toxic polyneuritis has been much used, but, as probably all polyneuritis is dependent on some toxin, its employment seems most appropriate for those cases in which the infective agent or the source of poisoning is not clearly established. Before dealing with these a few examples of rarer forms from the different groups may be referred to.

Silver is a very rare and probably doubtful cause of polyneuritis, the

[1] Presidential address delivered before the Neurological Section of the Royal Society of Medicine, October 12, 1922.

only case in the literature appearing to be that described by Gowers [13], of a man of 44 who took a dinner pill containing silver for about twelve years, averaging six pills a month. After eleven years cyanosis commenced to develop, and a year later wrist-drop, though as carcinoma of the liver declared itself some three months later, it is possible that the polyneuritis was to be accounted for by the toxæmia from the malignant disease.

Carbon bisulphide is a sufficiently uncommon cause of polyneuritis to justify a short description of a case I have had recently under treatment.

A boy, aged 15, worked at a boot factory at solutioning on rubber soles. He worked in a shed, which was afterwards described by the inspector as very badly ventilated, using for the purpose of fastening on the rubber soles a rubber solution containing carbon bisulphide. He worked from 8 a.m. to 6 p.m., and began to feel unwell in July, 1921, when he commenced to suffer from headaches almost every night towards the end of his work. The headaches were accompanied by vertigo, but had disappeared by the following morning. He informed me that previous workers at the same job had had to give it up on account of similar headaches and giddiness. He, however, stuck to his work, and in January of this year his right leg began to feel weak and to give way when walking towards the end of the day. This improved, and then the right hand grew weak and lost the power of gripping ; this also improved and the left hand became similarly affected. The headaches ceased in January just before the legs began to be affected. There was never at any time pain or numbness, or objective or subjective sensory symptoms. By the beginning of April he began to develop weakness of the dorsiflexors of both feet, being unable to raise the toes off the ground when standing, though the gastrocnemii were strong. Soon also bilateral weakness of the extensors of the fingers and wrists appeared, especially of the right extensor carpi ulnaris. Marked weakness and wasting of the right first dorsal interosseus and thenar muscles was also seen. To electrical testing there was well-marked reaction of degeneration in the extensors in both forearms, in the right first dorsal interosseus and in the tibialis anticus on each side. The knee-jerks were normal throughout, but the right Achilles jerk was absent, and the left only just obtainable with reinforcement. Treated with strychnine injections and massage he soon showed slight improvement, and after four months had practically recovered.

Carbon monoxide polyneuritis I have never met with, but it is said that a single severe dose of poisoning with this agent may be followed by neuritis, a very unusual feature in polyneuritis, which is usually the sequel of a more sustained or chronic poisoning. Care must, however, be taken in cases of carbon monoxide poisoning not to mistake pressure neuritis of the musculo-spiral, external popliteal or other nerve trunks

for toxæmic neuritis, pressure palsies being especially liable to occur in persons rendered unconscious by coal gas poisoning or by explosions in coal pits, through lying on a hard surface in one position for many hours.

Rheumatic polyneuritis.—Acute rheumatism or rheumatic fever is rarely if ever followed by polyneuritis, yet local perineuritis and fibrositis, as seen in brachial neuritis and sciatica, are common sequelæ of chill and exposure, though other causes frequently contribute, such as dental or intestinal sepsis.

Chloretone has been given extensively in children for chorea, and has been observed to produce a condition of flaccid paralysis, with absent deep reflexes, but the recovery on cessation of the drug is usually much more rapid than is usually met with in other forms of polyneuritis.

Local *asymmetrical neuritis* of definite nerve trunks rather than a symmetrical polyneuritis, is also a feature of typhoid and paratyphoid infections. Thus, a man of 29 with paratyphoid, a week after admission to hospital developed severe pains in the upper arms and shoulders, which kept him awake, followed by marked paresis of the right serratus, latissimus, triceps, and extensors of the right fingers and thumb, and of the left deltoid.

Another case of asymmetrical severe neuritis of the right median, ulnar and musculo-spiral nerves occurred in a man aged 27, as the sequel of a febrile attack of uncertain origin with tonsillitis, followed by acute nephritis. There was never any peeling of the skin to suggest scarlet fever, and bacteriological examinations for diphtheria, enteric and paratyphoid were negative. Possibly the infection was rheumatic, as nephritis is one of the rarer complications of this disease. After two weeks he had severe pains in the right arm from the shoulder to the hand, completely losing the use of the arm, and anæsthesia of the hand up to the wrist. The hand became very clawed and atrophic, and the finger pads and skin wasted, but practically complete recovery took place in two years. These asymmetrical forms of toxic neuritis are generally painful, perhaps owing to the inflammatory nature of the lesions affecting the interstitial tissue of the nerves, whereas in the symmetrical polyneuritis without sensory phenomena the lesion is probably purely a parenchymatous degeneration of the nerve elements themselves.

Asymmetrical neuritis of toxic origin may occasionally be met with in chronic alcoholism and diabetes. Musculo-spiral paralysis I have

many times seen occur in chronic alcoholism, when the element of pressure could apparently be excluded as a cause. In none of these cases of musculo-spiral palsy was pain a feature of the case, but in the sciatic and external popliteal paralyses met with in diabetes severe pain may be a prominent feature, preceding and accompanying the paralysis. It is difficult to understand how a local asymmetrical neuritis can be set up by the action of a circulating toxin, which should presumably act equally and symmetrically on both sides. The fact that certain whole nerve-trunk areas are liable to be affected in the asymmetrical forms is suggestive of a local interstitial neuritis being present rather than a degenerative parenchymatous neuritis, and this is further supported in my opinion by the fact that these asymmetrical forms are usually intensely painful. It is possible therefore, if not indeed probable, that the circulating toxin is not the direct factor in the development of the neuritis, but that it has led to the local appearance of an inflammatory interstitial neuritis, such as may result from chill and other so-called rheumatic processes.

The actual nature of the circulating toxin in such apparently simple cases as alcoholic or diabetic multiple neuritis is obscure. In all probability it is not alcohol itself or derivative ethers circulating in the blood that sets up alcoholic neuritis, or this disease would surely be commoner than it is, but rather a secondary auto-toxæmia produced by the action of the chronic alcoholism upon the tissues, notably on the digestive tract and the liver. Similarly in diabetes it can scarcely be the direct action of hyperglycæmia on the nervous structures that sets up local or multiple neuritis, nor is it due to acetone or diacetic acid, as both of these substances may be absent in cases of diabetic neuritis. Probably the neurotoxin in diabetes is of the autotoxæmic deficiency type, as will be referred to later.

The polyneuritic psychosis described by Korsakow [22] as common in chronic alcoholism with polyneuritis is certainly met with in other forms of polyneuritis, as Korsakow himself showed, and must therefore not be accepted as evidence that alcoholism is the cause of an obscure polyneuritis. Some two years ago I had the opportunity of watching throughout to its fatal ending a case of polyneuritis of unknown origin, in which the delusions and characteristic disorientation of time and space familiar in Korsakow's psychosis were very marked.

A man, aged 55, hall porter, early in September, 1920, began to suffer from severe pains in the left hip. After a fortnight he had to give up his work,

and three weeks later pains appeared in the right hip. On October 16, he was admitted under my care into St. Mary's Hospital as a supposed case of sciatica. There was some loss of power in both legs, and tactile anæsthesia of the feet and ankles, but no loss of power or of sensation in the arms or hands. Both knee-jerks and Achilles-jerks were absent, the plantars flexor. No glycosuria or albuminuria. Wassermann test of blood and c.s.f. both negative. On October 26, the electrical reactions were normal, but on November 5, definite reaction of degeneration had appeared in the left dorsiflexors, and peronei in both legs. By November 12, bilateral foot-drop was well marked, and there was retention of urine, daily catheterization being necessary. His mental condition had gradually become unreliable, and by this date delusions were very marked; he muttered to himself, and replied in the most extravagant manner to questions as to where he had been recently, such as to New York yesterday, and to Jerusalem the day previously, though he would otherwise answer questions quite rationally. He had always consistently denied the imputation of alcoholism, and I was able to convince myself by personal interviews with his wife and with his fellow employees at the Town Hall where he was porter, that his statements on this point were true. Irregular pyrexia developed towards the end of October, and he steadily got weaker and more torpid, dying on December 14. No post-mortem was permitted.

In another case, a man, aged 45, had a severe attack of polyneuritis, with intense pains in his feet and legs, with loss of the deep reflexes, and considerable delirium. Alcohol as a cause could be excluded. He later recovered all his muscular power, and the knee-jerks returned, but there was considerable permanent loss of memory and mental power, indicating the co-existence of an acute encephalitis with the polyneuritis.

Septicæmia is a not uncommon cause of multiple neuritis, differing little in type from alcoholic neuritis. The source of infection may be a quite insignificant wound; in two cases I saw well marked multiple neuritis follow slight local suppuration due to a grazed skin wound of the hand, and in another case due to a stab wound in the thigh. In one of them an early symptom was loss of ocular accommodation, which is such a common early symptom in post-diphtheritic neuritis.

Septicæmia is a not uncommon cause of multiple neuritis following childbirth or a miscarriage; one of the most severe and painful cases I have ever seen, ending in death from heart failure, occurred in an otherwise healthy girl of 23, after a miscarriage at three months, in all probability an artificially induced abortion. The polyneuritis which has been described as following tetanus is almost certainly of septicæmic origin, rather than due to tetanus toxin, though chloretone used in the treatment has been blamed in one case. I have seen the use of anti-streptococcic serum followed by a severe external popliteal paralysis; a

gunshot wound necessitated amputation of the foot, but on account of sepsis three doses of antistreptococcic serum were given on three successive days, and then after four days interval another dose. General joint pains all over resulted, followed four days after the last injection by pains in the right leg, dropped foot and wasting of the leg, with total paralysis of the extensor longus digitorum and of the peronei. It is doubtful whether this was septicæmic neuritis, or an effect of the serum.

Septicæmic neuritis may affect a nerve trunk close to the intervertebral foramina, as in a case of a gunshot wound of the left arm, followed four weeks later by pains in the opposite arm and right side of the neck, with paresis of the right serratus magnus and winged scapula, and hypo-æsthesia of a cutaneous strip from the ball of the thumb along the outer forearm and up to the shoulder, suggestive of neuritis of the sixth cervical nerve.

Generalized polyneuritis affecting all four limbs, with ataxy and loss of the knee-jerks, has been recorded by Clayton [9] in a soldier treated for typhoid by fifteen injections of 50 c.c. each of antityphoid serum. Here again it may be asked whether the polyneuritis was a result of the serum injections, or was it due to the typhoid toxin? My own view is that the neuritis is not the result of the serum treatment, but of the previous toxæmia, just as polyneuritis following diphtheria, whether treated with serum or not, should certainly be laid to the credit of the diphtheritic toxin.

A rare form of polyneuritis with facial diplegia has been described by Feiling [12] and others accompanying *parotitis* and *uveitis*, or polyneuritis may follow parotitis alone.

Acute febrile polyneuritis, first described by Osler [29], was frequently observed during the Great War, and cases were recorded by Gordon Holmes [21], Bradford [6], and others. The sequence of the polyneuritis to definite malaise and pyrexia places this type definitely in the infective rather than in the autotoxæmic group, though the exact source of the toxin has not yet been determined. Facial diplegia was a common symptom in this type of polyneuritis.

I saw a medical officer, just home from France early in 1919, who complained of pains in the left side of the neck, with soreness to touch, as though bruised, and almost immediately aching appeared in both forearms; three days later insomnia, and the arms became weak and the hands shaky. After three weeks facial diplegia developed, with a feeling of intense depression and malaise, with furred tongue, though no pyrexia was detected at any time.

There was a good deal of pain with hyperæsthesia and tenderness of the backs of the forearms, but no actual muscular paralysis. The knee-jerks were present throughout, and the legs were unaffected. There was never any sensory loss, and recovery was complete after three months.

Syphilis as a cause of polyneuritis is usually included in the cachectic group, but occasionally it undoubtedly acts as an acute infective toxæmia.

A man, aged 30, acquired syphilis in January, 1910. Three months later he developed some ataxy and numbness of the feet, but recovered. In October the numbness and ataxy returned with rapid onset of weakness of legs and arms, but again almost completely recovered under injections of salicylate of mercury. In January, 1911, twelve months after the original infection, weakness and wasting of the hands and feet began, which steadily progressed to complete paralysis of all muscles below the knees, with bilateral finger-drop and wasting of the forearm muscles.

All the deep reflexes were lost, but there was no trace of anæsthesia.

By November, 1912, he was recovering fair power in the gastrocnemii, and he could walk fairly with a stick. The hands were now normal, and the knee-jerks had returned, but there was no trace of power in any of the anterior tibial muscles, nor any reaction in them to either form of electrical current. Probably the correct interpretation of this case would be a polyneuritis associated with considerable anterior horn cell damage in the fifth lumbar region.

In considering the etiology of an attack of multiple neuritis in a syphilitic subject, the possibility of arsenical neuritis should not be overlooked if treatment by any of the arsenobenzol preparations has been given.

Tubercle as a cause of polyneuritis has been much discussed, the usual verdict being that such polyneuritis is mainly alcoholic, though the added stress of the tubercular toxin or cachexia, when combined with the chronic alcoholism, much increases the liability to degeneration of the nerves, just as alcohol in addition to arsenic, sepsis with rheumatism, and many other doubly acting causes may combine to produce it. Except when associated with another factor, tubercle is a very rare cause of neuritis. I have seen one case of generalized polyneuritis in a man dying from miliary tuberculosis, with no history of alcoholism or other ascertainable cause.

Tubercular neuritis of the feet.—In two cases of severe and fatal tubercular infection, I have seen symmetrical pains and wasting of the intrinsic musculature of the feet, with glossy skin. The first case had

been diagnosed as gout, in spite of extensive pulmonary tuberculosis, by no less an observer than the late Sir William Broadbent in 1895, and remembering this case when I saw the identical condition of the feet seven years later in a woman with obscure renal disease and pyrexia, I confidently diagnosed tubercle as the cause, though no one else agreed with me until the autopsy confirmed this.

In a few cases I have seen tubercular pleurisy followed by intensely severe *brachial neuritis* on the same side, with glossy skin and articular disorganization of the phalanges. Probably this is produced by apical infection of the lung and pleura setting up a secondary inflammatory neuritis in the brachial plexus in its close proximity.

Severe chronic anæmia is usually included among the *cachectic* causes of polyneuritis, though it appears to be much rarer than the spinal degenerations of combined sclerosis met with in conjunction with grave anæmia of pernicious type. I published last year [19] a case of *leukæmic polyneuritis*.

A youth, aged 17, developed well-marked symmetrical polyneuritis, with foot-drop, absent deep reflexes and sensory diminution on the feet and legs, as well as tingling and numbness of the finger-pads. His spleen was enlarged three finger-breadths, but there was no leucocytosis, indeed a leucopenia of only 5,800, but the cell count was notably inverted, the polymorphs being only 23 per cent. and the lymphocytes 68 per cent. Slight enlargement of the glands in the neck appeared, and one of these was removed for pathological examination, but was reported to be normal. Troublesome hæmorrhage from the wound continued at intervals, again suggestive of leukæmia, and he died six weeks after admission into hospital, three months after the first appearance of weakness of the legs.

Microscopical examination of the liver, kidneys and peripheral nerves showed these tissues to be infiltrated with lymphocytes, yet it is difficult to conceive that the symmetrical polyneuritis could be due to pressure of the lymphocytic exudation upon the nerve fibres; it was more probably of toxic origin due to some unknown form of autotoxæmia connected with the leukæmic process.

Malignant disease is also included amongst the cachectic group of polyneuritis, though it seems to be rare.

A year ago I saw a civil engineer, aged 69, who had been operated on seven years previously for malignant growth of the ascending colon, a short circuit being performed. He recovered well, and for years lived an ordinary life, travelling a great deal. In October, 1921, he thought he caught a chill, followed by pains in the left shoulder, arm and forearm, "like a rat gnawing it." The pains spread across the back of the neck and then affected the right

forearm, being so severe as to necessitate morphia. When I saw him in December there was complete paralysis of both triceps, and of the extensors of the fingers and ulnar extensors of both wrists, though the radial extensors of the wrists and the supinator longus of each side were normal; both serratus magnus muscles were very weak. There was a large mass in the right hypochondrium, which was shown at operation to be growth in the ascending colon with most extensive involvement of the liver. The legs were unaffected and the knee-jerks brisk; there was no glycosuria.

The distribution of the polyneuritis in this case was most unusual, with bilateral finger-drop and total paralysis of both triceps muscles, the legs being quite unaffected. The intensity and long duration of the pain were also striking features of the case. Possibly chill contributed to the onset of the neuritis, but the duration of three months with increasing symptoms was more suggestive of a continually acting toxin or cachexia, and is better explained by the extensive carcinoma from which he was suffering.

Autotoxæmia.—Perhaps the most interesting group of causes of polyneuritis is that I have labelled "autotoxæmic." We are constantly meeting with cases in which the closest investigation can elucidate no cause for the polyneuritis. One is tempted therefore to look upon them as autotoxæmic, though the Scotch verdict of "not proven" would be more correct.

An unmarried woman, aged 47, a school teacher, early last November began to suffer from burning pains in the legs, the feet becoming numb two months later, with loss of power of walking. There was some swelling of the hands due to rheumatoid polyarthritis, which also involved the left knee-joint. She complained of pins and needles in the fingers, and developed finger-drop owing to paresis of the extensor communis, and weakness and wasting of the intrinsic musculature of the hands. There was tactile anæsthesia and analgesia of the left hand up to the wrist, but no objective loss of sensation on the right hand, though she said it did not feel natural. There was complete left foot drop and some weakness of the right dorsiflexors. She could move the right but not the left toes. Though the right foot was much stronger than the left, there was much denser anæsthesia of this limb, extending to just above the knee. The knee-jerks were both brisk and equal, the Achilles-jerks were absent, and the left forearm flexor jerk absent too, though the right was brisk. After two months the pains in the legs increased considerably, and she complained of a curious subjective sensation "as though she had several pairs of legs in bed." This continued for several weeks. Now, after eleven months, there is some improvement in the muscular power of the legs, but she is still only just able to walk. There was a perforation of the nasal septum, suggestive in appearance of old syphilis, probably congenital, but the Wassermann reaction in the blood was negative.

It was difficult to assign the cause of this polyneuritis, though I incline to look on it as *rheumatic polyneuritis*, in view of the presence of painful multiple joint swellings, and the asymmetry and painfulness of the affection.

Beri-beri was at one time considered to be an infective polyneuritis due to a bacterial poison, but the more recent view ascribes it to a deficiency of vitamines in the diet, due to the eating of polished rice; the husk of the grain, which is thus lost to the diet, containing all the vitamins. Such a deficiency can act indirectly only, by setting up changes in the metabolic processes of the tissues, and thus probably the production of some insufficiently broken-down excretory product, which in the course of circulation affects the peripheral nerves, causing symmetrical parenchymatous degeneration. The process may be compared to that in diabetes, in which the lack of the normal internal secretion of the cells in the islands of Langerhans in the pancreas so alters normal metabolism that an excess of dextrose is produced in the breaking down of the muscular tissue. Yet it is probably neither the dextrose in the blood, nor the acetone or diacetic acid by-products, which are the actual toxic agent in producing the neuritis. In diabetic neuritis there may be symmetrical numbness and anæsthesia of the extremities, with loss of deep reflexes, but little or no muscular paresis, though there is well marked ataxy, the so-called diabetic pseudo-tabes. In another form the pains may be extremely severe, and the muscular paralysis well marked, often in the distribution of one sciatic, external popliteal or anterior crural nerve. Why a circulating toxin should thus set up an asymmetrical neuritis is hard to understand; it is usual to explain it by inferring a locally acting cause in addition, such as overuse or strain of the limb, or undue pressure on the nerve. In the asymmetrical neuritis of rheumatism or of paratyphoid fever, the asymmetry may be due to local involvement of the nerve sheaths by direct organismal infection, as in leprous neuritis, but in diabetes no organisms are known to be at work.

Puerperal neuritis.—Polyneuritis developing shortly after childbirth, or even during the puerperium, is sometimes considered to be a septicæmic neuritis, due to sepsis acquired during parturition, or to retained septic products in the uterus from a previous pregnancy. I do not think that this explanation will cover all the cases of polyneuritis associated with pregnancy, but rather that some are true cases of autotoxæmia, the toxin which produces the polyneuritis being elaborated in the tissues as an abnormal by-product of the metabolism in pregnancy.

A year ago I had under my care for some months a young married woman aged 30, who ten weeks after childbirth complained of weakness of the legs and of numbness, and of pins-and-needles spreading in the feet and hands, followed by numbness of the abdomen and chest up to the neck. All the deep reflexes were lost, and she was unable to lift the legs off the bed; the extensors of the fingers also became weak, but the extensors of the thumbs and of the wrists were unaffected. Bilateral facial palsy and diplopia next appeared, followed by diaphragmatic palsy for several days.

There was deep tenderness of the calves and forearms, and well-marked anæsthesia of the feet and ankles, but she never suffered from any spontaneous pains. There was never any pyrexia or recognizable sepsis after the childbirth. She recovered completely after four months.

Ten years ago Batten [5] showed at a clinical meeting of this Society a woman with recurrent paralysis and wasting of the hands and legs, with absence of the deep reflexes, the paralysis recurring after two confinements. Such recurrent paralysis will be referred to presently as having been observed in other cases of apparently autotoxic polyneuritis.

Pressure neuritis as a cause of paralysis following childbirth must be carefully distinguished from toxic polyneuritis, the nerve that usually suffers being the sciatic, and especially its external popliteal portion, from pressure of the fœtal head upon it near its exit from the pelvis at the sciatic notch.

Cranial nerve paralyses are common as a sequel of ordinary pharyngeal diphtheria, the third, fourth and sixth nerves being commonly affected, and occasionally the seventh, fifth, tenth and twelfth. The loss of accommodation due to paresis of the ciliary muscle, that is such an early sign in post-diphtheritic palsy, I have also seen in septicæmic neuritis and in one other case of toxic polyneuritis. Walshe [43] has pointed out that the frequency of incidence of cranial nerve paralyses after diphtheria is dependent on the close contiguity of the source of the toxin in the pharynx, as, in cases of polyneuritis following accidental diphtheritic infection of an open wound of the trunk or limbs, cranial nerve paralyses are uncommon.

A definite syndrome has been claimed for *polyneuritis cranialis*, many observations being recorded of neuritis limited to several cranial nerves. Oppenheim [28] thinks these cases are usually due to a basal process involving the cranial nerves. Kinnier Wilson [44] showed at the Clinical Section a man who, after right-sided otitis media of three weeks duration, developed nerve deafness, of the right ear, right facial palsy, paralysis of the right half of the soft palate and of the right

vocal cord, glosso-pharyngeal anæsthesia and hemiatrophy of the right half of the tongue, with bilateral loss of taste.

Slow chronic polyneuritis is a term that may be applied to cases in which the symptoms gradually increase during many months. Pain is usually either absent throughout, or only trifling at the commencement, but the muscular paralysis becomes extreme, and there may be extensive atrophy.

In the case of a man, aged 31, the symptoms gradually increased during twelve months, commencing with pain in the calves and a tired feeling, after the appearance of some large purpuric blotches on the legs.

The legs gradually became enfeebled to the stage of total flaccid palsy, the hands and forearms not being involved until nine months after the commencement of symptoms. When I saw him seventeen months after the onset, there was practically complete palsy of the feet and legs, hands and wrists, with contracture of the feet and hands. All the deep reflexes were lost and there was considerable anæsthesia in the periphery of all four limbs. The sphincters were normal, and no cause suggestive of polyneuritis could be discovered. Wassermann test negative in both blood and cerebrospinal fluid.

A girl, aged 15, became gradually weaker during twelve months until all four limbs were totally paralysed: she could not raise the head from the pillow, the eyelids and lips were partially paralysed, there was weakness of the masticatory muscles, and the tongue was somewhat wasted No sensory symptoms were present at any time except slight paræsthesiæ of the fingers at the commencement. All the deep reflexes were lost, but only slight muscular wasting occurred, and no contractures. No improvement was observable in spite of daily massage and electrical treatment until eighteen months after the onset, when she slowly began to regain power, and ultimately recovered perfectly in another two years.

The slow development of the symptoms in such cases strongly suggests a continuously acting toxin, rather than an acute poisoning, and one is driven to the supposition that an autotoxæmia is at work. In the girl's case at least the continual absorption of external toxins could be excluded, as her first symptoms occurred when at school in South Africa and advanced for three months at home some distance away, and she continued to get weaker for another nine months after being sent to England.

Relapsing and recurrent polyneuritis.—The commonest causes of recurrent polyneuritis are chronic alcoholism and lead poisoning, but recurrence is also met with in cases where the cause is obscure. F. G. Thomson [42] recorded the case of a youth of 19 in whom weak-

ness commenced in the hands and feet five days after being thrown out of a sculling boat; within another ten days there was complete paralysis of all four limbs and of both sides of the face, with considerable weakness of the trunk muscles. The sensory symptoms were confined to slight numbness of the fingers and the soles of the feet. All the deep reflexes were lost and considerable wasting developed later in the muscles about the shoulders, forearms and legs, the extensors being chiefly affected. Recovery was complete in every respect in about two years. An interesting fact in the history was that this boy at the age of 5 years had had apparently a similar attack of motor paralysis affecting all four limbs, ending in complete recovery in eighteen months. The acuteness of the onset of the paralysis following the immersion is strongly suggestive of chill being the exciting factor, though his previous similar attack at the age of 5 seems to demonstrate a predisposition in his metabolic processes to the development of a neurotoxin, or possibly an excessive sensitiveness of his peripheral nerves to the action of such neurotoxin.

In lead poisoning it seems to be established that a recurrence of wrist-drop and colic may be dependent upon some slight cause, as a febrile attack or an irregularity in diet, in the total absence of any fresh source of lead absorption. This fact lends support to Mary Sherwood's suggestion [36], that the first attack of neuritis leaves the nerves with a lowered power of resistance to the assault of a fresh toxæmia.

Grocco [15] was the first to describe recurrent attacks of polyneuritis in the absence of any obvious cause such as lead or alcohol. Other reports of such cases have been made by Eichhorst [11], by Mary Sherwood [36], who described two cases from Eichhorst's clinic in Zurich, though her first case was that of recurrent palsy of the right arm only, and should scarcely be classed with other cases of generalized multiple neuritis. Ross and Bury [33] describe two sisters with recurring paralysis. Targowla [40] recounts the case of a woman who had three attacks of paralysis at the ages of 19, 27, and 39 years. Sorgo [37] described the case of a man who after three attacks of abdominal pain and constipation developed bilateral palsy of the arms, followed twelve months later by a recurrence of the paralysis and colic, and again eight months later following a chill, colic, severe pains, paralysis of the arms, weakness of the legs, loss of the knee-jerks, respiratory paralysis and death. Degenerative neuritis was found in

the peripheral nerves. The sequence of the paralysis to attacks of severe abdominal pains and constipation is suggestive of an enterotoxin having been the cause, and is strikingly similar to the mode of onset of the paralysis in acute hæmatoporphyrinuric polyneuritis.

H. M. Thomas [41] published a clinical lecture on Recurrent Polyneuritis, describing the case of a man of 28, who had five attacks of paralysis within six years. In his case chronic indigestion was a feature of the illness, and possibly here also an enterotoxin was the cause.

A somewhat similar case was published by Nattrass [27]; a boy aged 18 developed double foot-drop, loss of deep reflexes, and other signs of generalized multiple neuritis, who had had two similar attacks of paralysis lasting for several months, one at the age of 4 and the other at 17. A pecularity in his case was enlargement and tenderness of the nerve trunks, especially of the median, ulnar and external popliteal.

Hæmatoporphyrinuric polyneuritis.—In 1908 my attention was first drawn to this curious syndrome:—

A woman, aged 47, was admitted to St. Mary's Hospital with pains in the abdomen, following a cold three weeks previously. Her pulse was 120, and the urine was noticed to be dark reddish coloured, hæmatoporphyrinuria being found on analysis. A week later she began to complain of pains all over her limbs and body, and it was found that she could not raise her arms to the level of the shoulder. The pains were worst in the arms and shoulders, but there was no anæsthesia. In five days she was unable to sit up or to feed herself. Insomnia became troublesome, and there was retention of urine, with overflow incontinence. The pains in her arms were so severe that she complained of feeling as if the skin was being torn off. The knee-jerks were present on admission, but were afterwards lost for some weeks. Three months later she could just hold out her arms, but there was still complete paralysis of the extensors of the fingers on both sides, with reaction of degeneration, though the extensors of the wrist and supinator longus were unaffected. Ultimately she recovered completely, the hæmatoporphyrinuria having disappeared before she left hospital.

It was not until February 1921 that I met with another case of this disease.

A man, aged 45, well nourished and living in perfect conditions in the country, apparently in perfect health except that he had always been obstinately constipated, was seized with pains in the back. Next day his urine was dark red coloured. The pulse was 60, and he now complained of severe pains around the loins and the front of the abdomen, at first thought by his doctor to be renal colic and then an acute abdomen, for which he was

sent into a nursing home and a surgeon fetched from London. The latter however, refused to operate, making a diagnosis of acute pancreatitis. All the next week his pains were severe, and he was said to be jaundiced, and to have bile in the urine. On the fourth day there was retention of urine requiring use of the catheter. After eleven days he became excitable and nervous, owing to which I was asked to see him. The pulse was then 100, the strength of limbs and trunk good, and he could stand and walk. The knee-jerks were normal, as were all the other reflexes. He complained of some paræsthesiæ of the trunk, and, taken with his excitable nervous condition and sleeplessness, I thought he was developing acute mania. There was no history of venereal disease and his cerebrospinal fluid was normal. Two days later I saw him again; he could still stand, but the knee-jerks were now absent, and there was no weakness or anæsthesia. He again had retention of urine, and on the doctor passing the catheter I was astonished to see that the so-called bile-stained urine was port wine coloured, an extreme example of hæmatoporphyrinuria. Three days later he complained of "deadness" of the chest and abdomen when touched, and large areas in this region were found to be analgesic. Paresis of the deltoids was now well marked, as well as weakness of the flexors of the hips, but no other weakness of the limbs. His rectal temperature was now for the first time slightly raised; two days later his temperature was 100° F. and the pulse 132. He was now much weaker, unable to turn in bed and to cough owing to weakness of the abdominal muscles. The constipation became more and more extreme, the diaphragm paralysed, and he died after an illness of three weeks' duration. Unfortunately an autopsy was not permitted.

Needless to say, in both these cases sulphonal and other drugs as a possible source of poisoning were excluded. In both acute abdominal pains were amongst the earliest symptoms, followed immediately by hæmatoporphyrinuria, pains all over, paræsthesiæ and paralysis, especially of the arms, loss of knee-jerks, retention of urine and insomnia. In neither of my two cases was vomiting noted.

Hæmatoporphyrinuria may occur with symptoms of acute illness quite unconnected with the taking of any drug; it was first described in a case of acute rheumatism by MacMunn in 1880 [26], under the name of urohæmatin.

Acute attacks are ushered in by severe pains in the abdomen and loins, constipation, and sometimes vomiting. Dark-brown to port-wine coloured urine is an early symptom, and the pains continue and may spread all over the trunk and limbs. The pulse-rate is raised to 100 or 120, but usually there is no pyrexia. Retention of urine and even incontinence may occur, and occasionally mental symptoms may be noticeable, such as general nervousness, excitability, or even delirium and epileptic fits.

Gunther's excellent article [17] quotes fourteen cases in the literature, in four of which severe paralysis rapidly developed, followed by death soon after the onset of the paralysis, the earliest recorded case being that of Ranking and Pardington in 1890 [31].

These observers described the cases of two single women aged 41 and 47, both living in the same house, who were both taken ill with hæmatoporphyrinuria within a week; both were extremely neurotic, dyspeptic and constipated.

In the first case the symptoms followed immediately after a large dose (20 gr.) of acetanilide had been given in three doses within four hours. Partial suppression and retention of urine, which was port-wine in colour, followed immediately, and death occurred a week later, the legs being paralysed for a day before death. Their second case developed no paralysis and recovered, though the symptoms otherwise were similar. It is difficult to believe the possibility of simple coincidence for such a rare condition as hæmatoporphyrinuria in these two cases, in the absence of some common factor, as a drug, of which however there is no record, except the excessive dose of acetanilide in the first case.

Schulte [34 described the case of a ship's cook, aged 35, who was seized with abdominal pains, hæmatoporphyrinuria, followed by typical multiple neuritis affecting the arms only, paresis of the deltoids, biceps, supinator longus, infraspinatus and the extensors in the forearms. The pulse was only 48, there was no pyrexia and the man recovered.

Bachlechner [2] has recorded a case of hæmatoporphyrinuria followed by symmetrical wrist-drop and foot-drop, with the reaction of degeneration, in which the paresis developed with two succeeding attacks of the acute symptoms; and Gunther [18] states that repeated attacks of the syndrome of acute hæmatoporphyrinuria may occur within a year, though in none of his own cases did polyneuritis develop.

L. F. Barker and Estes [3] observed a girl aged 18 with hæmatoporphyrinuria and polyneuritis which ended fatally after sixteen months. She passed dark urine for the whole of that time, and suffered from pain in the lower abdomen, recurring nausea and vomiting, vertigo and epileptic fits. Laparotomy disclosed a dilated pylorus and duodenum. Two months later, after complaining of severe pains all over, bilateral wrist and foot drop developed, with extensive muscular atrophy, including the intrinsic hand muscles. The deep reflexes were at first exaggerated but later lost, and she died four months later. At the autopsy there

was found great distension of the stomach and duodenum. A very interesting point in this case was that the family history disclosed the fact that four other members of the family seemed to have suffered similarly with hæmatoporphyrinuria and nausea with abdominal pains, one of her sisters having died after being ill for nine months with similar symptoms. The strong family tendency to these symptoms, associated with hæmatoporphyrinuria, is practically conclusive evidence of an autotoxæmia being the origin of the syndrome. In all probability an intestinal toxin is to blame. Barker and Estes regard the gastro-duodenal dilatation as primary, the toxæmia producing the hæmatoporphyrinuria and polyneuritis being secondary. In my second and fatal case the obstinate constipation was a striking and troublesome symptom from which he had always suffered, and it is suggestive that the toxæmia was intestinal in origin.

Gunther applied the term acute toxic hæmatoporphyrinuria to those cases in which the symptoms follow chronic poisoning by sulphonal, trional, tetronal, veronal or its derivatives. Lead, saffron and glycerine, are also said to produce toxic hæmatoporphyrinuria.

Hæmatoporphyrinuria resulting from the use of sulphonal was first observed by Stokvis [39], in the case of a woman who passed port-wine coloured urine after taking sulphonal for many months. Schulz [35] described a fatal case after taking 15 gr. of trional daily for one month, the symptoms being epigastric pain and vomiting, and followed by loss of strength two weeks later, hæmatoporphyrinuria appearing for a few days before death. Many cases of this acute sequel of chronic sulphonal or trional poisoning have since been published, and in about one-fourth of them acute paralysis has been noted. The syndrome closely resembles that of acute hæmatoporphyrinuria not due to drugs. Thus, severe abdominal pains, vomiting and constipation, are often prominent symptoms, recovery rarely happening when all these three symptoms are present. A typical case was described by Anson [1]. A woman, aged 35, after taking 30 gr. of sulphonal daily for three and a half years, developed acute abdominal symptoms, constipation, hæmatoporphyrinuria, intense pains in the legs, loss of knee-jerks, followed ten days later by marked weakness of the legs, increasing to total paralysis, the arms being later similarly affected. There was no anæsthesia, but incontinence of both sphincters until death. In this case no toxic symptoms appeared until the drug had been taken regularly for three and a half years, but in other cases the symptoms have come on acutely after even one or two doses of trional or sulphonal.

In Keith Campbell's case in 1897 [7], in the Royal Asylum, Perth, a domestic servant, aged 22, nervous and depressed, and suffering from constipation, was given two powders of 15 gr. each of sulphonal and phenacetin. Vomiting commenced four days later, and hæmatoporphyrinuria fourteen days after taking the drugs. Convulsions developed as well as nystagmus, progressive paralysis, loss of the knee-jerks, and death occurred thirteen days after the first vomiting.

Stockton [38] described a case of acute ascending paralysis with hæmatoporphyrinuria in a girl, aged 27, who, previously strong and healthy, became obstinately constipated, and twelve months later nervous, irritable and anæmic. She was given three doses of 5 gr. each of sodium salicylate and sulphonal. Vomiting set in, the pulse became slow and the urine claret coloured. Fifteen gr. of sulphonal was given and next night a similar dose of trional, but both failed to induce sleep. Anæsthesia of the buttocks appeared, followed by incontinence of both sphincters, shooting pains in the legs, progressive paralysis and anæsthesia, the arms being last affected, and loss of the knee-jerks. Some power returned in the feet and legs but the arms remained totally paralysed, and there was total loss of sensation on the trunk and lower limbs. Doubtful optic neuritis was observed before death. No autopsy was obtained. In the discussion on this paper, Putnam [30] referred to a case of his own of increasing paralysis with hæmatoporphyrinuria following the administration of sulphonal, in which degenerative neuritis was discovered at the autopsy, the spinal cord being normal.

A case of hæmatoporphyrinuric polyneuritis following the use of trional was published in 1901 by Hart [20], in which recovery occurred. Trional differs from sulphonal only in the substitution of an ethyl group, C_2H_5, for a methyl group, CH_3. His patient was a woman, aged 50, who had taken much trional for a long time, when acute colicky abdominal pain with nausea and vomiting developed. There was no pyrexia, abdominal tenderness or distension. Five days later hæmatoporphyrinuria appeared, followed within a week by progressive paralysis of the extensors of the feet and wrists, with severe pains, anæsthesia and loss of deep reflexes. There was delirium and psychosis of Korsakow type. The pains in the limbs and abdomen were excruciating for a time, and limb contractures developed, followed by a slow recovery.

REFERENCES.

[1] Anson. *Brit. Med. Journ.*, 1920, **1**, 634.
[2] Bachlechner. *Diss. Erlangen*, 1914.
[3] Barker and Estes. *Journ. Amer. Med. Assoc.*, 1912, **59**, 718.
[4] Barnes. *Brain*, 1902, **25**, 479.
[5] Batten. *Proc. Roy. Soc. Med.*, 1912-13, **6**, Neurol. Sect., 62.
[6] Bradford, Bashford and Wilson. *Quart. Journ. Med.*, 1918-19, **12**, 88.
[7] Campbell. *Journ. of Ment. Science*, 1898, **44**, 305.
[8] Caspari. *Zeitsch. f. klin. Med.*, 1882, **5**, 537.
[9] Clayton. *Amer. Journ. Med. Sci.*, 1915, **149**, 706.
[10] Duménil. *Gaz. Hebdomadaire*, 1864, sér. ii, **1**, 203.
[11] Eichhorst. *Correspondenzbl. f. Schweizer Aerzte*, 1890, **20**, 429.
[12] Feiling and Viner. *Journ. of Neurol. and Psychopath.*, 1922, **2**, 353.
[13] Gowers. "Diseases of Nervous System," 2nd ed., 1893, **2**, 967.
[14] Grinker. *Journ. Amer. Med. Assoc.*, 1907, **48**, 849.
[15] Grocco. "Contrib. allo studio clin. e anat. path. d. nevrite multiple primitiva," *Ann. Univ. di Med. e Chir.*, Milano, 1885, **271**, 3.
[16] Grund. *Zentralbl. f. inn. Med.*, 1919, **40**, 810.
[17] Günther. *Deutsch. Arch. f. klin. Med.*, 1912, **105**, 89.
[18] *Idem*. *Ibid.*, 1920, **134**, 257.
[19] Harris. *Lancet*, 1921, **1**, 122.
[20] Hart. *Amer. Journ. Med. Sci.*, 1901, **121**, 435.
[21] Holmes. Osler and McCrae's "System of Medicine," London, 1910, **7**, 522.
Idem. *Brit. Med. Journ.*, 1917, **2**, 37.
[22] Korsakow. *Arch. f. Psych.*, 1890, **21**, 669.
[23] Langdon Brown and Williams. *Lancet*, 1909, **1**, 1105.
[24] Leyden, von. *Zeitsch. f. klin. Med.*, 1880, **1**, 405.
[25] Löffler. *Correspondenzbl. f. Schweizer Aerzte*, 1919, **49**, 1891.
[26] MacMunn. *Proc. Roy. Soc.*, 1880, **31**, 211.
[27] Nattrass. *Journ. of Neurol. and Psychopath.*, 1921, **2**, 159.
[28] Oppenheim. "Text-Book of Nervous Diseases," Eng. Trans, Edinb., 1911, 5th ed., **1**, 515.
[29] Osler. "Principles and Practice of Medicine," Edinb.-Lond., 1892, ed. i, 777.
[30] Putnam. *Trans. Assoc. Amer. Phys.*, 1900, **15**, 10.
[31] Ranking and Pardington. *Lancet*, 1890, **2**, 607.
[32] Remak and Flatau. Nothnagel's "Specielle Path. u. Therap.," Wien, 1900, Bd. **11**, Theil 3.
[33] Ross and Bury. "Peripheral Neuritis," London, 1893.
[34] Schulte. *Deutsch. Arch. f. klin. Med.*, 1897, **58**, 313.
[35] Schulz. *Deutsch. med. Woch.*, 1894, **20**, 152.
[36] Sherwood. *Virchow's Archiv*, 1891, **123**, 166.
[37] Sorgo. *Zeitsch. f. klin. Med.*, 1897, **32**, Suppl., Heft 223-255.
[38] Stockton. *Trans. Assoc. Amer. Phys.*, 1900, **15**, 6.
[39] Stokvis. *Ned. Tijdschrift v. Geneesk.*, 1889, **25**, pt. 2, 409.
Idem. See also *Zeitsch. f. klin. Med.*, 1895, **28**, 1.
[40] Targowla. *Rev. neurologique*, 1894, **2**, 465.
[41] Thomas. *Philadelphia Med. Journ.*, 1898, **1**, 885.
[42] Thomson, F. G. *Brit. Med. Journ.*, 1910, **2**, 1443.
[43] Walshe. *Quart. Journ. Med.*, 1918-19, **12**, 14.
Idem. *Brain*, 1920, **43**, 74.
[44] Wilson, S. A. K. *Proc. Roy. Soc. Med.*, 1919-20, **13**, Clin. Sect., 64.

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ON MUSCLE TONUS.

DE BOER'S EXPERIMENT ON THE FROG.

(From the Physiological Laboratory, Utrecht.)

BY J. W. LANGELAAN.

DE BOER'S experiment consists in cutting the rami communicantes which unite the sympathetic chain with the spinal nerves of the lumbar plexus. After their section the frog is fixed in a clamp by means of a hook through the nose, as was first done by Brondgeest. When hanging in this way the difference in position and in length of the two hind legs can be observed. In these experiments the frog was always intact, that is the spinal cord was not divided. According to de Boer the leg on the side on which the rami communicantes are cut is invariably more extended and slightly longer than that of the normal side, and he attributes this difference to a loss of tonus of the muscles of this limb. He states that the loss of tonus in this case is as complete as after the section of the posterior roots of the lumbar plexus. This effect, according to de Boer, is permanent, and he concludes that muscle tonus is governed exclusively by the sympathetic system, and that the impulses maintaining tonus reach the muscles by way of the rami communicantes.

The same experiment repeated on the cat has yielded similar results. The definition which de Boer gives of tonus is the same as that of Johannes Müller, Brondgeest, and the great majority of recent investigators, viz., a state of slight contraction of muscle.

In repeating this experiment I performed the operation as carefully as possible. The frog was rendered motionless by being wrapped in cotton wool and the needles which fixed the animal pierced the wool only. The intestines were always kept within the abdominal cavity and pushed aside by means of a little tampon moistened in Ringer's solution. The blood-vessels were spared as far as possible, especially the large vena dorso-lumbalis (Gaupp). Before reaching the rami communicantes, the parietal peritoneum must be incised and in most cases the kidney pushed a little aside. In this latter manipulation, as well as during the section of the rami communicantes, it is difficult to

avoid stretching the sympathetic chain and its branches. The stretching of these nerves increases and lengthens the period of shock following the section of the rami.[1] The same effect is produced by bringing the intestines outside the body in order to facilitate the operation; most observers have done so and consequently produced severe and prolonged shock of the spinal reflex arcs.

I have performed the operation in every case on the right side only upon male frogs of moderate size. The operation is much more difficult in *rana temporaria* than in *rana esculenta*, and in many other respects too the former is not so suitable for the experiment. I usually divided the rami communicantes uniting the sympathetic chain with the seventh, eighth and ninth spinal nerve trunks, but in some cases the sixth ramus was also sectioned, and in others the tenth.[2] The latter ramus is very slender and does not seem to influence the muscles of the hind limb. As the wound must be carefully sewn up, this part of the operation took approximately a quarter of an hour and consequently I never observed the animals earlier than ten to fifteen minutes after the section of the rami communicantes.

Rana esculenta survived the operation well for several weeks, after which the animals were then killed for the purpose of autopsy; *rana temporaria*, however, stood the operation badly, suffered from severe shock and often died within the course of a few days. I think this was chiefly due to the bad state in which the animals reached the laboratory during this year.

When a normal frog is suspended by means of a hook piercing its nose, its first act is a defensive movement. By placing its feet against the hook and then stretching its extremities with force, it tries to free itself from it. A small drop of a 3 per cent. solution of cocaine upon the wound through which the hook passes often suppresses these movements. As soon as the defensive movements cease flight movements appear. In *rana esculenta* swimming movements are more common, whilst in *rana temporaria* jumping movements prevail. In its natural state a frog performs two different kinds of swimming movements; ordinary swimming, that is symmetrical and synchronous movement of the four legs, and alternating swimming movements. As soon as the

[1] The term "shock" is used for that temporary suppression or depression of nervous function which follows immediately upon mechanical injury of some part of the nervous system.

[2] The spinal nerve leaving the cord between the first and second vertebræ is reckoned as the first spinal nerve.

fore-part of the body meets an obstacle when swimming in the ordinary way the movements become alternate; then the extended right fore-limb is flexed and adducted to the chest, and the flexed and adducted left hind limb is extended with force. These movements alternate with the reverse movements of the contralateral limbs; they are slower and less strong than the symmetrical swimming movements. On reaching land this alternating movement insensibly develops into creeping. Alternate swimming is, therefore, the transition between swimming and creeping, or it is a creeping movement in water. The jumping movement is always symmetrical, consisting chiefly in a forced extension of both hind limbs. All these movements are slightly modified when the frog is suspended, but in general they are easily recognized.

In my experiments the hook that pierced the nose was not attached immediately at the clamp, but was held by another hook fixed into the clamp. This arrangement allowed rotation to occur round the vertical axis as soon as the animal executed a movement which was not strictly symmetrical. Most observers using the suspension method of Brondgeest seem to have attached their animals in a similar way, so that there is scarcely any doubt that the reflexes caused by these rotations hampered their observations. The rotation movements which occur in my arrangement have in general a small amplitude and a quickly increasing and decreasing angular velocity. The frog is said to rotate clockwise when the rotation is in the same direction as the hands of a watch placed with the dial plate upwards; when the movement is reversed we say that the frog rotates anti-clockwise.

Such a rotation stimulates both labyrinths simultaneously but not to the same degree. Clockwise rotation stimulates chiefly the left labyrinth, anti-clockwise the right. The two labyrinths act synergically in the reflex movements they produce; these are most marked in the hind limbs, but they occur in the fore limbs too. The movements of the hind limbs are chiefly extension and flexion; the extension movement begins with spreading of the toes, combined with forced extension of toes and foot, followed by extension at the knee-joint and later by abduction of the whole leg from the middle line, combined with a slight ventral adduction at the hip-joint. The flexion movement commences with adduction of the toes, associated with flexion of toes and foot; then flexion at the knee-joint, followed by adduction of the whole leg towards the middle line, and a slight dorsal adduction at the hip-joint. The extension movement of the fore limb commences with a

slight spreading of the fingers, followed by extension of the arm and abduction from the body. The flexion movement begins with a slight adduction of the fingers, associated with flexion of the arm and adduction of the whole limb against the chest. The reflex movements resulting from the rotation of the suspended animal are shown in the following synoptic table.

ANIMAL ROTATING ANTI-CLOCKWISE (RIGHT LABYRINTH CHIEFLY STIMULATED).

Right labyrinth	Hind limb	Right, forced extension.
		Left, flexion.
	Fore limb	Right, extension.
		Left, flexion.
Left labyrinth	Hind limb	Right, extension, weak or absent.
		Left, slight flexion.
	Fore limb	Right, extension, weak or absent.
		Left, slight flexion.

When the animal rotates clockwise it is the left labyrinth which is chiefly stimulated, and the resulting reaction may be deduced from the table by interchanging right and left.

The movements elicited reflexly from the labyrinths are rather slow and are executed with considerable force. They commence in the toes and foot of the same side as the labyrinth which is stimulated by the rotation, so that when the animal turns clockwise it is the toes of the left foot which first spread. If the stimulus is weak, or the threshold high owing to the exhaustion of the reflex, the only obvious reaction is the spreading of the toes, the slight extension of the limb often escaping our attention.

The reflex elicited by the rotation of the suspended frog was first described and recorded photographically by Dusser de Barenne [7], who proved its labyrinthine origin. This reflex must not be confounded with the automatism provoked by suspending the frog by means of a twisted string, so that the animal turns slowly and always in the same direction. Like all reflexes in the suspended animal, the rotatory seems to be a normal reflex, for if we imagine the animal in its natural position with its four legs touching the ground the extension of the limbs of one side would check rotation round its cranio-caudal axis. According to the researches of Quick [16], this is the normal reflex movement elicited in all vertebrates by stimulation of the semicircular

canals. The rotation reflex is therefore probably a normal labyrinthine reflex, slightly modified by the suspended position of the animal.

When the animal has been suspended for some time, the irritability of the semicircular canals is increased owing to the abnormal position, and consequently even a slight degree of rotation is followed by a reflex movement. It is not possible to eliminate the reflex by suspending the frog by a single hook, since rotation may still occur owing to the elastic nature of the tissues in which the hook is fixed; under these conditions the excursions are greatly diminished and easily escape our attention, and we may be therefore deceived by the reflex movements provoked by them.

When the intact frog is suspended the defence automatism is the predominant reaction, and when it is eliminated the rotary reflex usually prevails. As soon therefore as flight movements produce a slight rotation of the animal, they are suppressed by the rotation reflex. If the spinal cord of the frog is divided between the second and third spinal roots the defence and the rotatory reflexes are abolished, and the flight reflexes prevail. The swimming and jumping movements, however, have no longer the same precision as in the intact animal, and are often arrested before the apparent aim of the movement is attained; in other words, the automatism subsides into a simple sequence of spinal reflexes.

It has been pointed out that the difference in the position of the two hind limbs may be rendered more evident by immersing the frog in water. Water being a dense medium of approximately the same specific density as the tissues, the tensional stresses existing in the muscles have free play to develop their strains when the animal is immersed. But water, in consequence of its density, also restricts movements, which consequently either do not occur, or cease earlier than they would in air. But the reactions observed when the suspended frog is immersed may not be the normal ones, since the immersion may act as a physiological stimulus. If the frog is lowered slowly and at a uniform rate and no farther than the middle of its body, into water of exactly the same temperature as the room, the immersion seems to have no stimulating effect, but if these precautions are neglected swimming movements are often elicited. Immersion into water of much lower temperature than the room seems to increase the flexion of the hind legs, but not to influence extension. This method therefore introduces many sources of error and cannot be considered an improvement. The suspension of a normal frog by a hook is also an unsatisfactory

method, and I should not have employed it if the question whether efferent sympathetic nerves influence the tonic state of the muscles had not been raised by de Boer's experiments performed by it.

In an earlier publication [10] I tried to show that muscle tonus depends upon two different properties of muscle, and that these two properties are governed by two different sets of efferent nerves. Shortly afterwards and independently, Pieron [14] [15] came to the same conclusion. The first property of the tonic muscle is plasticity. A body is said to be plastic if its form is permanently altered when a stress to which it is subjected is removed. It follows from this definition that if the body was in a state of equilibrium before the deformation, it will be again in equilibrium after the deformation. If, therefore, the form of a plastic muscle is altered for a moment by the action of internal or external forces, the deformation produced by these forces is partly permanent. The greater the permanent deformation in comparison with the total change of form, the more plastic the muscle. Hence, if a muscle contracts a shortening remains, while if it is extended by the action of its antagonists a lengthening is the result; whereas a muscle which has lost its plasticity returns after each change of form to the same definite length. It is evident that a permanent deformation in a muscle is not attended by a continued expenditure of energy nor accompanied by rhythmic electric phenomena, while the production of a permanent deformation, or a variation in an existing deformation, is accompanied by the expenditure of free energy and by electric phenomena[1]. Plasticity, I believe, is intimately connected with what is usually called the "trophic state" of the muscle, and the degree of plasticity may possibly therefore prove to be a measure of the trophic state of muscular tissue.

Plastic tonus is that state of the muscle in which it has the properties of a plastic body. This term is chosen to indicate that the plasticity of muscle is maintained and controlled by the central nervous system. As shown in an earlier publication [7], an isolated muscle may be deprived of its plasticity by physical disturbances of the same kind as occur during the normal function of the muscle. There is, therefore, no doubt that the maintenance of plasticity is a function of the central nervous system. Hence, plastic tonus is a reflex tonus. It shows itself not so much during movement as after movement. It influences therefore the attitude of the animal, and its diminution or

[1] Electric phenomena have been observed by de Meyer [12] in non-permanent deformation of muscle.

loss must alter normal postures. Sherrington, especially [17] in his article on reflex postural activity, called attention to this function of the tonic muscle. During movements plastic tonus influences the steadiness of the movement, and its diminution or loss is revealed by unsteadiness of movement.

The second property of the tonic muscle is the faculty of maintaining a state of slight contraction. This property of muscle I proposed to call *contractile tonus*. It is the reflex tonus of Johannes Müller, Brondgeest, de Boer and of most of modern authors; it is now generally admitted that it is maintained and controlled by the central nervous system. When in a state of contractile tonus the muscle is not in equilibrium, but in a state of slight contraction. For this reason the maintenance of the contractile tonus is accompanied by the expenditure of free energy and by rhythmic electric phenomena; and it is therefore intimately connected with heat production, especially in the homoiothermic animals. The view that reflex tonus comprises two components is in harmony with recent morphological researches of Boeke [1], as well as with the researches of Wertheim Salomonson [18] on the electric phenomena of tonic muscle.

In order to avoid confusion, I will use the word "tonus" as the general term, comprising the two components, plastic and contractile tonus. The part played by each of the two components in the joint results is left indeterminate. The terms "plastic tonus" and "contractile tonus" will always be used strictly in the sense defined above.

The first group of experiments was made on intact frogs, the spinal cord not being cut. The seventh, eighth and ninth rami communicantes were divided on the right side. As soon as the animal is released, a quarter of an hour after the operation, it immediately regains its natural position and jumps away; when placed in the basin it swims. The voluntary movements seem almost normal, but the animal, when jumping or swimming, often deviates a little from the straight line. On squatting immediately after having made a jump, the attitude is abnormal (fig. 1). The trunk deviates to the left, the right hind limb is abducted from the body, the knee points laterally and the foot is not covered by the leg; the area of the limb in contact with the ground is larger than on the normal side. It is evident, on examining the mid-dorsal line, that the superior part of the trunk forms an obtuse angle with the inferior part. Below the level of this angle on the right side the papillæ of the skin are flattened and the skin itself is darker. On

the photograph reproduced in fig. 1, these changes, characteristic of loss of function of the sympathetic system, are very striking upon the trunk, but they exist also, though less distinctly, upon the right hind limb. When the animal sits quietly the curvature of the trunk gradually diminishes in the course of some minutes, but a slight deviation remains. The abnormal position of the hind limb is usually also corrected, but as this correction takes place abruptly it gives the impression of volitional movement. The slight deviation of the trunk at rest persists for a period of four to six weeks, and then disappears in

FIG. 1.—Normal frog (*R. esculenta*). Section of the seventh, eighth and ninth rami communicantes on the right side; photograph on the following day to show the attitude of the animal three minutes after having made a jump.

consequence of gradual compensation, which may go so far as to lead to slight deviation of the trunk to the opposite side. As I will show later, it is impulses emanating from the left labyrinth which bring about this compensation. As soon as the frog comes to rest and floats upon the water after swimming, the right hind leg is not adduced to the body, but remains partly extended and hangs down (fig. 2). Sometimes extension is the most striking feature, at other times it is drooping of the leg. In consequence of this abnormal attitude, the frog no longer floats symmetrically, but the right half of the body, and especially its posterior part, is more submerged. When floating quietly this abnormal position may persist for a long while, but it is usually

corrected, apparently volitionally, in the course of some minutes. The abnormal attitude of the hind limb is permanent and may be observed for several weeks after the operation (fig. 3); complete

FIG. 2.—Normal frog (*R. esculenta*). Section of the seventh, eighth and ninth rami communicantes on the right side on December 27, 1921. Photographed next day as the animal floated on water. The right side of the body is more deeply submerged, and the right hind limb hangs down.

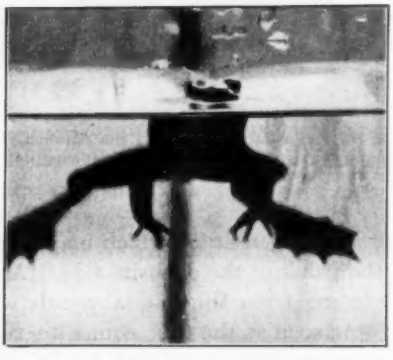

FIG. 3.—Normal frog (*R. esculenta*). Section of the seventh, eighth and ninth rami communicantes on the right side on January 4, 1922. Photographed on January 28, 1922, as the frog floated in water; front view. The right half of the body is more deeply submerged, and the right hind limb is more extended and hangs lower. Same animal as in fig. 4.

compensation did not occur in the course of my experiments. These different abnormal postures are easily observed in *rana esculenta;* in *rana temporaria* they are often absent shortly after the

operation in consequence of local shock, and later they are mostly obscured by the restlessness and lively movements of these animals.

When the frog is suspended immediately after the operation[1] the right hind limb is extremely flabby, more extended and slightly longer than the normal one. The flabbiness of the limb is the most striking phenomenon and is always present. It may be demonstrated by quickly moving the frog to and fro; then the right limb swings more easily, the amplitude of its movement is larger and it continues to swing after the normal limb has come to rest. If jerked up and down its movements are irregular, whereas the normal limb moves more smoothly. The flabbiness of the musculature is also shown by the form of the leg (fig. 5). The calf is flattened and the pretibial muscles hang down along the bone so that their greatest prominence is slightly lower than on the normal side. Similar differences may be observed between the two thighs. The flabbiness of the hind limb gradually diminishes in the course of the first day after the operation, but then remains approximately unchanged for at least two months. What happens after this period I do not know.

On comparing the attitudes of the hind limbs when the frog is suspended during the first hour after operation, it is evident that the right limb is more extended and that the right foot droops. The increase in the length of the limb is chiefly due to this abnormal position of the foot. When measured by means of a horizontal microscope it amounts to approximately 3 to 4 mm. in a middle-sized frog of about 185 mm. in length from nose to toe. In some cases the difference may reach 5 mm. immediately after the operation. If the animal is then carefully immersed in water the difference in the position of the legs becomes more obvious, and the flabbiness of the limb is more evident, for even the slightest vibration of the fluid is communicated to it, whilst the normal leg remains at rest. Some time after the operation the difference in position and in length of the two legs begins to diminish. If the operation was performed carefully recovery sets in within an hour, but if done roughly it may persist several hours. At the end of the first day, a state is usually reached which seems stationary for several days, till compensation becomes perceptible. In this stage, the difference in length between the two legs amounts to 1·5 to 2·5 mm. when the animal is hanging quietly.

[1] The descending root of the nervus trigeminus reaches the lumbar region of the cord in the frog. If, therefore, the hook piercing the nose deviates a little from the middle line, e.g., to the right, flexion reflexes may be evoked in the right hind limb by stimuli emanating directly from the wound made by the hook.

In experiments in which the operation happened to be easy and stretching the sympathetic chain and the rami communicantes could be avoided, I observed that immediately after the operation the right limb was more flexed and shorter than the normal one, but in the course of the first hour it became slightly more extended and longer than the left as the animal was hanging quietly. In these cases the final elongation never exceeded 2·5 mm. I am inclined to believe that in this instance the local shock was very slight, and that the section of the rami communicantes may have acted as a stimulus.

As soon as the frog is suspended immediately after the operation it usually makes defence movements. When this reaction to its abnormal position has ceased spontaneously or is suppressed by a drop of cocaine solution, the rotatory reflexes and those elicited from the skin are either abolished or strongly diminished on the right, and often slightly depressed on the normal side too, in consequence of the local shock produced by the section of the rami communicantes. The degree of depression of the reflexes depends chiefly upon the manner in which the operation was performed; if easy the depression is slight and of short duration; if, on the other hand, difficult and attended by stretching of the sympathetic chain, the depression is deep and prolonged. The first reflex that can be elicited is always the rotatory reflex. It reappears during the first hour after the operation and long before the stationary state is reached, in which the elongation of the right hind limb amounts to no more than 1·5 to 2·5 mm. It is evident, as the local shock is disappearing, that the reflex movements provoked by the stimulation of the right labyrinth are diminished, so that the movements evoked from the left labyrinth become preponderant. The depression of the function of the labyrinth on the side on which the rami communicantes are cut remains permanent during the whole period of observation, and one gets even the impression that the predominance of the left labyrinth increases rather than decreases. A glance at the table on p. 437 will make it clear that the predominance of the left labyrinth causes extension to prevail in the left hind limb and flexion in the right hind limb (fig 4). Moreover, the abnormal position of the animal increases the irritability of the labyrinths, so that even the slightest and hardly perceptible rotation provokes a reflex movement. As a result of the manner in which the animal is suspended there is probably no active movement which is not accompanied by a rotatory component, and the labyrinths are therefore incessantly stimulated. The rotatory reflex, as already said, is strongly dominant, and therefore after each active

movement of the animal the right limb is temporarily shortened and the left limb temporarily extended. This is the reason why Dusser de Barenne [6] observed shortly after the operation that the hind limb on the side on which the rami communicantes are severed is shorter than that on the normal side. It is only during the period of local shock, when the rotatory reflex cannot be elicited, or at the moments when the labyrinthine reflexes are exhausted, or, finally, when the animal has been hanging quietly for at least a quarter of an hour, that the elongation following section of the rami communicantes

FIG. 4.—Normal frog (*R. esculenta*). Section of the seventh, eighth and ninth rami communicantes on the right side on January 4, 1922; photographed January 25, 1922. The flexion of the right hind limb when suspended is due to predominance of the left labyrinth. The same animal is shown in fig. 3.

can be observed in the frog in which the spinal cord is intact. I have also tried to demonstrate the difference in function between the two labyrinths by placing the frog upon a rotating disk. The correction movements, however, are chiefly executed by the head and those parts of the trunk lying above the level where the rami are divided. The method afforded, therefore, no definite results.

The reflexes that return next are those elicited from the skin. The first to appear is the simple flexion reflex, quickly followed by swimming movements, especially in *rana esculenta*, and by jumping movements in *rana temporaria*. The swimming and jumping movements often appear quasi-spontaneous. From the first moment that all these reflexes

reappear, it is evident that the movements of the right limb lack steadiness; they resemble in this respect the movements in locomotor ataxia. This unsteadiness is a consequence of the diminution of the plasticity of the muscles, and may be observed for at least several days after the operation. For the same reason the deformation of the muscle after a contraction or after stretching is diminished on the right as compared with the normal side. The right hind limb, having executed a movement, returns, therefore, more nearly to its inherent equilibrium length than the normal one. It follows from these considerations that the difference in length of the two hind limbs, as soon as the local shock has passed away, is not a fixed quantity, but depends chiefly upon what happened just before the limbs were at rest. Owing to the predominance of the rotatory reflex the right hind limb is more likely to be shorter at a moment arbitrarily chosen than the normal one. This fact was actually observed in the frog by Yas Kuno [9] and by Negrin y Lopez in co-operation with von Brucke [10], in the cat. It was erroneously considered by these observers as being in contradiction with de Boer's observations.

Summarizing the result of this group of experiments, we conclude: *Section of the seventh, eighth, and ninth rami communicantes in the frog is followed by local shock of the primary reflex arcs of the spinal cord. During the period of shock, the loss of tonus is complete (de Boer [2]). As soon as the shock has passed off the loss of tonus is only partial (Dusser de Barenne [6]). As a result of section of the rami communicantes, the muscles lose a great deal of their plasticity. The diminution of the plasticity of the muscles shows itself most distinctly in the attitudes of the animal, but the movements also lack steadiness. The results of diminution of plasticity are gradually compensated by stimuli emanating from the labyrinths, especially from the labyrinth opposite the side on which the rami communicantes are divided.*

The second group of experiments was also made on intact frogs. In this group, the seventh, eighth, and ninth posterior roots were divided on the right side. As soon as the animal is released, approximately a quarter of an hour after the section of the roots, it regains its natural position. The attitude of the animal is normal, with the exception that the right hind leg is flabby and trails behind the body in consequence of local shock produced by the section of the roots. In the course of the first half-hour after the operation the leg begins to flex slightly and

to adduct a little to the body. When in this period of recovery the animal floats upon the water in a basin, the hind limb is flexed, and brought almost into its normal position. At the end of the first day the right hind limb is still a little flabby. When the animal is squatting, the hind limb, in consequence of this flabbiness, projects a little from the body, and a greater surface of the leg touches the ground than on the normal side. Owing to the same reason the right heel is lower than the left. Sometimes the leg is more flexed than normal at the knee and the ankle joints, especially when the animal sits after having made a jump. This deviation from the normal position occurs only after the movement described by Hering [8] as the "tilt phenomenon." If the operation has been successful and local shock slight, the state of the animal immediately after it is approximately the same as it usually is at the end of the first hour.

When the animal is suspended directly the operation is terminated, the position of the right hind limb, as de Boer has stated, is exactly the same as it is after section of the rami communicantes. The difference in length between the two legs amounts at most to 5 mm. in a frog of normal size. This agreement in position and in elongation is due to the fact that in both instances the operation produces a severe local shock of the primary reflex arcs of the spinal cord, in consequence of which there is temporarily a complete loss of tonus. In the course of the first day after the operation, the difference in the position and length of the two legs diminishes, and finally the length of the right hind limb does not exceed the length of the normal one by more than 1 to 2 mm. This difference is still present a week after the operation. The rotatory reflex reappears within the first half-hour. At first the flexion and the extension of the right limb are somewhat feeble, but soon the difference between the reflex movements of the two sides is hardly perceptible. When the operation has produced but little shock, the rotatory reflex may be present from the first moment, and movement is almost normal—the only difference between the two sides being a slight diminution of the steadiness of the movement of the right limb. This unsteadiness is only perceptible during that phase of the reflex movement in which the foot is extended and the toes spread. When the animal has been suspended for a time even the slightest rotation provokes a reflex movement. This proves that the labyrinths become more irritable owing to the abnormal position of the animal.

Summarizing the results of this second group of experiments, we

may conclude: *Section of the seventh, eighth, and ninth posterior roots in the frog is followed by local shock of the primary reflex arcs of the spinal cord. During the period of shock the loss of tonus is complete, as Brondgeest has stated* [4]. *As soon as the shock has passed off, a diminution of tonus remains. The postures and movements of the animal are approximately normal, so that the diminution of tonus seems chiefly, though not exclusively, due to a decrease of contractile tonus. The rotatory reflex is not permanently influenced by section of the posterior roots.*

The third group of experiments was made on frogs in which the spinal cord had been divided between the second and third spinal roots. When the animal is released, approximately ten minutes after the section of the cord, it usually regains its squatting position when put upon the table in the proper manner. Its posture, however, is more crouching than it was before. Recovery from shock begins in the course of the first day after the section, and then the reflexes gradually reappear. When the animal is suspended, the loss of tonus produced by the shock is complete in the distal part of the body; the hind limbs are flabby and the heels often touch each other. As soon as recovery sets in the tonus returns, at first in the more proximal parts of the limb, later in the foot and the toes. The reflexes that may now be elicited are the flexion and swimming reflexes. The irritability of the preparation increases as the shock passes off, so that the slightest touch of the skin, or even an insignificant jar, elicits a reflex. Flexion movements now prevail, since the extension reflex emanating from the labyrinth is abolished. In consequence of the predominance of the flexion movements the permanent deformation of the muscles is in the same direction, and so the well-known flexion contractures develop.

When the shock following the section of the spinal cord has largely subsided, approximately twenty-four hours after the operation, the seventh, eighth and ninth rami communicantes are divided on the right side. The local shock following the section is usually not so severe as when the cord is intact. The phenomena which may be observed in the suspended animal are qualitatively the same as when the cord is intact. When tonus returns the right hind limb remains flabby and is slightly longer than the normal (fig. 5). The difference in length, however, never exceeds 1 to 1·5 mm., and usually amounts to 1 mm. only. As this slight difference in length is not very obvious, it is the flabbiness of the hind limb and the unsteadiness of its move-

ments which more clearly reveal the diminution of plasticity. The flabbiness of the limb, though diminished, still exists on the tenth day after the operation; I did not observe the animals for a longer period. The unsteadiness may be demonstrated by gently squeezing the two feet simultaneously; then the hind legs are raised and adducted to the body as if the frog were sitting, but the right limb is not so much adducted as the left, and falls abruptly when giving up this position. The left hind limb maintains the position somewhat longer and then falls slowly, often by steps. When the right leg is actively extended

FIG. 5.—The spinal cord was transected 1·5 mm. below the calamus scriptorius on January 9 at 1 p.m. At 1.30 p.m. division of the sixth, seventh, eighth, ninth and tenth rami communicantes on the right side. Photographed at 1.30 p.m. on the following day to show the difference in position and length of the hind limbs when the animal was partly immersed in water. The right limb—and especially its distal part—is surrounded by a halo, owing to slight vibration transmitted to this limb from the water; it affected this limb only.

the movement is also abrupt, and the leg often passes for a moment its position of equilibrium. On stimulating the two feet simultaneously, I often got the impression that the right limb, the rami communicantes to which were divided, was not so irritable as the other. I sometimes observed a slight, hardly perceptible flexion of the left leg occurring to all appearances spontaneously; and while in this flexed position, which may be maintained for several minutes, the reflex irritability of

the leg was considerably increased, so that even touching the foot with the point of a fine human hair provoked a vigorous flexion reflex. I have the impression that this slight flexion of the leg is the same phenomenon as the shortening of the muscle which always precedes a muscle clonus [11]. In both instances, I believe, the shortening is due to impulses reaching the muscle from the sympathetic system. In several experiments the succession and the interval of time between the two operations was varied, but the chief results were always the same.

Summarizing the results of the third group of experiments, we may conclude: *Section of the spinal cord between the second and third spinal roots is always followed by severe shock in the distal part of the body. During the period of shock the loss of tonus is complete, and when the shock has passed, a diminution of the tonus remains. Subsequent section of the seventh, eighth and ninth rami communicantes produces a diminution of the plasticity of the muscles of the hind limb. After the section of the spinal cord, the rotatory reflex is abolished.*

The fourth group of experiments was made on frogs in which the spinal cord was only partially cut through. The experiments in which the section of the spinal cord between the second and third spinal roots was proved by autopsy to be incomplete, taught that the rotatory reflex, though feeble, may still be elicited if the external part of the antero-lateral tract and the zona marginalis only are left intact. A certain number of fibres subserving the reflex reach, therefore, these regions of the spinal cord at the level not below the second spinal nerve.

In another set of experiments the more lateral region of the medulla oblongata, 1·5 mm. above the calamus scriptorius, was cut through on one side. The more medial region of the oblongata, containing the fasciculus longitudinalis posterior, was always spared. I divided therefore the formation known in the higher vertebrates as the corpus restiforme. The effect upon the posture of the animal resembles that produced by the section of the rami communicantes, but is much more pronounced and extends over the whole side of the body on which the corpus restiforme is divided, so that when swimming or jumping the animal deviates considerably from the straight line, and when squatting the whole body is curved to one side. The rotatory reflex emanating from the labyrinth on the side on which the corpus restiforme is injured is abolished.

Summarizing the results of this fourth group of experiments, we may conclude: *The fibres conducting tonic impulses from the labyrinth to the muscles pass by the way of the corpus restiforme; a certain part of the fibres subserving the rotatory reflex enters the tractus antero-lateralis of the spinal cord.*

The results of this research have led to a scheme of the primary spinal reflex arcs which differs from the current conception. While I was completing this scheme, Bok [3] published his morphological researches

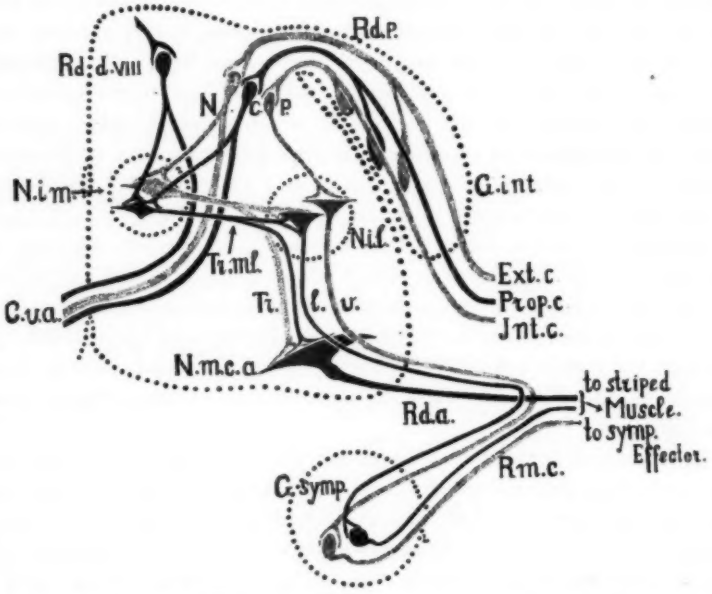

FIG. 6.—Scheme of the primary spinal reflex arcs. C.v.a., commissura ventralis alba. Ext.c., exteroceptor. G.int., ganglion intervertebrale. G.symp., ganglion sympathicum. Int.c., interoceptor. N.i.l., nucleus intermedio-lateralis. N.i.m., nucleus intermedio-medialis. N.m.c.a., nucleus motorius cornu anterioris. N.c.p., nucleus proprius cornu posterioris. Prop.c., proprioceptor. Rd.d.VIII, radix descendens nervi vestibularis. Rd.a., radix anterior. Rd.p., radix posterior. Rm.c., ramus communicans. Tr.l.v., tractus latero-ventralis. Tr.m.l., tractus medio-lateralis.

on the structure of the spinal cord. The results at which we had arrived independently agreed so closely that we have tried together to plan a scheme of the primary reflex arcs of the cord. In fig. 6 this scheme is reproduced. We started with the idea that the primary spinal reflex arcs subserve, in the first place, the more primitive spinal

reflexes. The primitive exteroceptive reflexes elicited from the skin are, in our opinion, the nociceptive withdrawal reflexes, of which the simple flexion reflex is the most common type. The primitive proprioceptive reflex initiated in the motor apparatus itself is tonus. The labyrinth, in as far as its impulses help to maintain tonus, we associate for well-known reasons with the proprioceptive system. The primary spinal reflex arcs are, we believe, homosegmental, at least in those cases in which the primitive segmental character of the sympathetic system is still preserved. When, however, the outflow of the sympathetic fibres from the central nervous system contracts and becomes confined to the thoraco-lumbal part of the cord, this primitive character of the primary reflex arc is of course modified. Assuming that the primary reflex arc in the lumbal region of the frog's spinal cord is still homosegmental, we reproduce in our scheme only those elements which appear in a sequence of cross-sections of a single spinal segment. The new fact incorporated in this scheme is represented by the nucleus intermedio-medialis. (Cajal [5], Bok [3].) By the intermediation of the cells of this nucleus the stimuli reaching the cord by way of the posterior roots are distributed over the efferent sympathetic cells of the nucleus intermedio-lateralis and to the motor cells of the anterior horn, reaching first the efferent sympathetic cells and then the motor cells of the anterior horn. The nucleus intermedio-medialis is, therefore, the final common centre of the primary spinal reflex arcs.

In order that this scheme may not be misunderstood we call attention to the fact that the more complicated combinations of movements, especially progression and active attitude, are initiated by stimuli emanating from centres lying above the medulla oblongata. The fibres connecting these centres with the spinal motor centres enter the antero-lateral tract above the level of the primary motor centres where they terminate. These fibres are present in large numbers, but have been omitted in the scheme as not pertaining to the primary spinal mechanism. For the same reason there have been omitted the labyrinthine fibres that enter the antero-lateral tract above the level of the second spinal nerve, as well as all intersegmental associative fibres.

On the basis of this scheme we may now say more precisely what is meant by the word "local" in the term "local shock." On dividing the rami communicantes it is clear that shock affects, in the first place, the sympathetic efferent section of the primary spinal reflex arc, i.e.,

the nucleus intermedio-lateralis, and that when it spreads it reaches the nucleus intermedio-medialis. Similarily division of the posterior roots causes, in the first place, shock in the afferent section of the primary spinal reflex arc, i.e., in the nucleus proprius cornu posterioris; then the shock extends to the nucleus intermedio-medialis. The fact that shock affects the nucleus intermedio-medialis after section of the rami communicantes, as well as on section of the posterior roots, is the reason of the close correspondence in the state of the animal immediately after those two operations.

In conclusion, I have to thank my colleague, Professor Zwaardemaker, who in the most courteous manner placed his laboratory at my disposal.

REFERENCES.

[1] Boeke, J. *Brain*, 1921, **44**, 1.
[2] de Boer, S. "De beteekenis der tonische innervatie voor de functie der dwarsgestreepte spieren," Amsterdam, 1914.
[3] Bok, S. T. *Psych. en Neurol. Bladen*, 1922, **26**, 174.
[4] Brondgeest, P. Q. "Onderzoekingen over den tonus der willekeurige spieren," Utrecht, 1860.
[5] Ramón Cajal, S. "Textura del sistema nervioso," t.**1**, Madrid, 1899.
[6] Dusser de Barenne, J. G. *Arch. f. d. ges. Physiol.*, 1916, **166**, 145.
[7] *Idem. Psych. en Nerurol. Bladen*, 1918, **22**, 258.
[8] Hering, H. E. *Arch. f. exp. Pathol. u. Pharmacol.*, 1897, **38**, 266.
[9] Kuno, Y. *Journ. of Physiol.*, 1914-15, **39**, 139.
[10] Langelaan, J. W. *Brain*, 1915, **38**, 235.
[11] *Idem. ibid.*, 328.
[12] de Meyer, J. *Arch. int. de Physiol.*, 1921, **16**, 64, 172, 193.
[13] Negrin y Lopez, J., und Brücke, E.Th. *Arch. f. d. ges. Physiol.*, 1917, **166**, 55.
[14] Piéron, H. C. R. *Soc. de Biol.*, 1918, **81**, 293.
[15] *Idem. Revue neurolog.*, 1920.
[16] Quix, P. H. *Nederl. Tijdschrift v. Geneesk.*, 1922, **66**, 1071.
[17] Sherrington, C. S. *Brain*, 1915, **38**, 191.
[18] Wertheim Salomonson, J. K. A. *Brain*, 1920, **43**, 369.

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THE CENTRAL CONNECTIONS OF THE VESTIBULAR NUCLEI WITH THE CORPUS STRIATUM, AND THEIR SIGNIFICANCE FOR OCULAR MOVEMENTS AND FOR LOCOMOTION.

BY L. J. J. MUSKENS, AMSTERDAM.

THE main facts about the cerebrofugal tracts have been known for some considerable time, but it is only of late that even a preliminary knowledge of the central ascending connections of the cerebral sensory nerves have been attained.

Monakow, Cajal, van Gehuchten, Probst, Horsley, O. and C. Vogt, and Sachs have pointed out the great importance of the thalamic nuclei as central stations for all corticopetal connections.

Wallenberg, Spitzer, van Gehuchten, and Hoesel were among the first to investigate the central connections of the more important sensory nerves—the N. trigeminus and N. vestibularis. As a result of these investigations a certain amount of light was thrown on the cerebropetal tracts of the N. trigeminus, but very little was learned about the central connections of the N. vestibularis. It is a curious fact that although physiological and anatomical data indicate the importance of these central connections, practically nothing was for long known about them. This is evident in Horsley's Boyle lecture of 1905, since in this lecture support is given to Mill's supposition that vestibular ascending connections arrive in the temporal convolutions. This view is, however, not accepted by Winkler, Kappers and Brouwer, who regard the lateral fillet as the pathway, or one of the pathways, for ascending vestibular stimuli to the higher cerebral centres. In 1914 [9] proof was forthcoming that the vestibular central connections pass upwards almost entirely in the posterior longitudinal bundle. A few pass from the nuclei tecti, where the cerebellar root of the vestibular nerve terminates, through the anterior cerebellar peduncle. Another tract may pass upwards from the nucleus ventralis raphé, but this is doubtful.

These few facts represented the sum of our knowledge of the central connections of the vestibular nuclei, and yet these connections are of the first importance for ocular movements, for equilibrium and for locomotion. Free locomotion and ocular movements in more than one plane are first seen in the lower vertebrates coincidently with the

appearance of a vestibular organ, or some comparable apparatus, and with the development of a primitive corpus striatum.

From the clinical aspect, the regular appearance of typical disturbances of equilibrium of the cerebellar type in cases of tumour of the brain, and the presence of nystagmus and conjugate deviation of the eyeballs in variously localized lesions of the cerebral axis, indicate unmistakably the existence of ascending tracts from the vestibular nuclei.

The extraordinary importance of the subject and our very meagre information seemed to me sufficient excuse for this paper describing my work on the central connections of the vestibular nuclei, even if it be as yet incomplete.

Before passing to a description of my work and its results I would point out that the anatomical-physiological methods adopted by me in this and in earlier work [9] are not yet recognized by other workers.

Observations were first made by a series of lesions in the brain-stem of the cat. It was found that only lesions of the posterior longitudinal bundle resulted in forced movements in the horizontal plane (circus movement and conjugate deviation of head and eyes) and in the frontal plane (rolling movements and squint deviation of the eyes). Lesions elsewhere in the brain-stem were never followed by these types of deviation or movement.

Further, it was found that the direction of those forced movements was reversed when the lesion (hemisection) reached the region of the posterior commissure, and the nucleus commissuræ posterioris and nucleus interstitialis. From my observations these nuclei form the termini for the ascending fibres of the posterior longitudinal bundle after they have crossed in the posterior commissure. From these nuclei also originate the two descending tracts in the posterior longitudinal bundle (tr. commissuro-medullaris and tr. interstitio-spinalis or Boyce's tract).

It was also observed that a unilateral lesion of structures oral to these nuclei, involving the strands of fibres between them and the globus pallidus, was also followed by forced movements in the reversed direction. This phenomenon seems to be best interpreted by the assumption that nervous continuity exists between the two commissural nuclei and the globus pallidus.

In connection with this last observation, it is interesting to note that C. and O. Vogt [21], whose work is on purely anatomical lines, have also come to this conclusion, that a direct nervous connection exists between the commissural nuclei of the one side and the globus pallidus of the other. This partial anatomical confirmation of facts obtained by me with the anatomo-physiological method seems to be a valuable

argument in its favour, and goes far to justify its adoption in attempting to trace the ascending vestibular tracts.

In an earlier paper [9] I pointed out that within the nuclear complex of the N. vestibularis in quadrupeds a very high degree of differentiation of function is attained. On each side of the median line are two nuclei, lesions of which cause circus movements but in different directions. Lesion of one of the nuclei produces circus movements to the same side, while lesion of the other is followed by circus movements to the other side. Injury of the tracts ascending from these nuclei to join the mesial part of the posterior longitudinal bundle also results in similar forced movements. Further, on each side of the median line lie two nuclei, injury of which causes rolling movements. These nuclei show the same differentiation as those associated with the circus movements, since a lesion of one results in the rolling movements being directed towards the affected side, while injury on the other is associated with rolling movements directed towards the opposite side. The ascending fibres from these two nuclei are localized in the lateral wing of the posterior longitudinal bundle.

It is important to note that in a cross section involving the whole of one longitudinal bundle, including as it does the fibres concerned with circus movements to both sides, the result is circus movement to the intact side, rolling movement to the affected side. If, however, the lesion is situated oral to the posterior commissure the circus movements and rolling movements are conversely directed towards the affected and the intact sides.

It is found in monkeys, cats and birds, that a lesion involving the nuclei tecti and their ascending fibres in the superior cerebellar peduncle is followed by the falling backward of the animal, or at least a conjugate deviation of the eyeballs upward. On the other hand if the lesion involves the grey matter near the raphé of the medulla (nuclei of the raphé) and the medial nuclei of the pons the result is a distinct tendency to fall forwards. Further, a lesion in this region of the human brain appears to be associated equally with nystagmus and a forced position of the eyeballs in the vertical plane.

Before passing to the main subject matter of this paper I would recall my earlier work of 1907 [8] where I demonstrated that the nucleus tecti receives direct as well as indirect fibres from the vestibular nerve. This was subsequently confirmed by de Villaverde [20]. These data on the anatomical, physiological relations of the vestibular nerve may form a basis for further investigation, for there is, as far as the Marchis-stain goes, evidence that no other ascending vesti-

bular pathways exist. Careful workers consider the lateral fillet as a possible pathway for secondary vestibular tracts. This view they regard as being phylogenetically sound.

In the evidence which I offer for the solution of the problem I shall confine myself to one case in which the experiment may be regarded as crucial.

The experiment, which was performed on a cat, was carried out as follows: A protected needle, as devised by Probst, was used to pierce the medulla. This was introduced from behind on the right side and manipulated so that the vestibular region was completely destroyed (figs. 1 and 2). The needle pierced the lateral fillet at the level of the mesencephalon. On examination it was found that all the tracts described by me as secondary vestibular tracts were degenerated (fig. 3). The lateral fillet was quite free from any degenerative change up to the point where the needle pierced it (fig. 4). From this point marked degeneration extended right up to the end station in the thalamus (fig. 5). I repeated this experiment several times with the same result, viz., no degenerative changes occur in the lateral fillet from injury of the vestibular nuclei.

The result of these experiments is, in my opinion, sufficient to justify the conclusion that the fillet contains neither primary nor secondary vestibular fibres.

The next point for investigation is whether the physiological method used in the anatomical analysis of the primary and secondary vestibular connections will serve equally well for the elucidation of the tertiary vestibular connections. By tertiary vestibular connections are meant those tracts which connect the supra-nuclear centres (i.e., the nucleus commissuræ posterioris and the nucleus interstitialis) near the posterior commissure with the prosencephalon.

Theoretically no objection can be raised to the method, but the fact must be remembered that the physiological effect of a lesion of the ascending vestibular connections diminishes markedly the farther it lies from the entrance of the vestibular nerve. A second point is that the resulting forced movements vary in degree in different animals. Thus in rabbits they are very vigorous, but are much less when the same experiment is performed on animals higher in the scale. Thus in man a lesion of the ascending tracts causes only a forced position of the eyes, or a still less impressive phenomenon, a tendency to conjugate deviation ("Blickparese" of the Germans), or a tendency to fall or walk to one side when the eyes are closed.

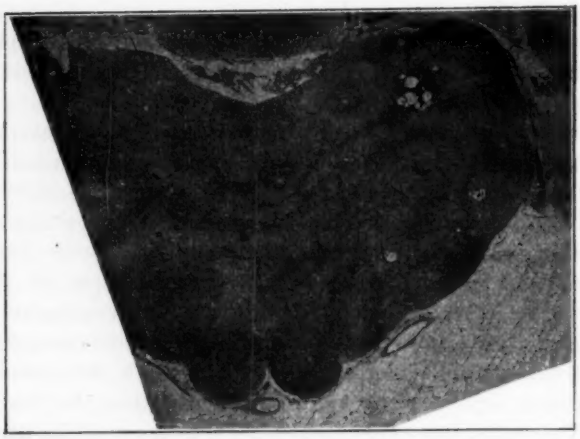

Fig. 1.

Fig. 2.

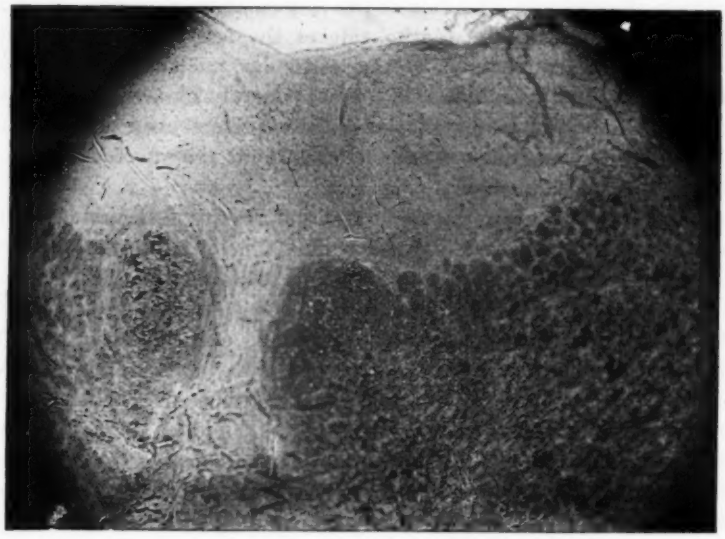

Fig. 3.

Fig. 4.

Fig. 5.

FIGS. 1-5.—Cat. Lesion of the vestibular nuclei. Ascending degeneration in the posterior longitudinal bundle only. Note absence of degeneration in the lateral fillet.

Again, in quadrupeds section of the vestibular nerve causes, as a rule, violent rolling movements to the side of the lesion, whereas a lesion of the ascending connections of the vestibular nuclei in the midbrain (posterior longitudinal bundles) is followed merely by a tendency to fall towards the affected side. In the human subject even this may not occur, but there is a tendency to lie in bed on the affected side, or to lean over to that side when sitting up.

It is, therefore, not remarkable that the result of severance of the tracts connecting the supranuclear centre (nucleus interstitialis) with the prosencephalon should be only a slight tendency to fall towards the normal side. It must be remembered, however, that this symptom although slight is very constant. Further, after a lesion in the prosencephalon in quadrupeds, the circus movements which result are neither so marked nor so persistent as those seen after section of the mesial portion of the posterior longitudinal bundle. Sometimes this circus movement to the side of the lesion may last a few days only, especially if the lesion be slight, but there may be a tendency for some time for deviation of the head and eyes towards the lesion. In monkeys and in man regular circus movements never result, but there is a distinct tendency to look towards the lesion. If the subject be blindfolded and told to march there will be seen a clear tendency to deviate from the straight line.

Regarding forced movements in the frontal plane, after prosencephalic lesions in quadrupeds there is a tendency to fall towards the normal side, accompanied by a deviation of the eyeballs known as the "Magendie-Hertwig squint." In man both these symptoms must be looked for very carefully, or they are completely missed. Careful observation is necessary to detect forced movements in the sagittal plane (forwards and backwards) in quadrupeds, while in man their observation requires special attention. Consequently the physiological-anatomical analysis of the tertiary vestibular connections has to be carried out with the utmost circumspection and critical care.

When we take into consideration how little is known of the physiology of the corpus striatum it is not surprising that its significance as a vestibular end-station has only recently been recognized. Remarks in the literature indicate that attention has been attracted to the corpus striatum in cases of conjugate deviation and forced movements. Prevost [12] calls attention to the fact that when in apoplexy the apoplectic area involves the corpus striatum, conjugate deviation of the head and eyes towards the side of the lesion results. Prus [14] notes that when

certain parts of the corpus striatum are stimulated electrically either pleurothotonus or elevation of the head results. Sachs [17] also records stimulation experiments of the same nature. Bechterew [1], who must be regarded as a pioneer in this work, records observations made by him of forced movements in dogs after lesions involving the base of the forebrain, and postulates the presence of vestibular centres in this region, although he does not mention the corpus striatum.

In experiments carried out by me on cats I found that lesions involving the region of the hypothalamus, the lamina medullaris ventralis and the globus pallidus were followed by circus movements to the side of the lesion and rolling movements to the normal side. Lesions involving other parts, as the anterior and median thalamic nuclei, or the anterior corpora quadrigemina, corpus geniculatum and corpus callosum, never gave rise to forced movements of any description.

The difficulties attending anatomical investigation of this region are very great. Dejerine and Horsley with their co-workers rendered valuable assistance to the investigation of nerve tracts by their application of the Marchi method. At the same time when an effort is made to extend the older physiological work of Majendie, Schiff, Probst and others, the difficulties, which of necessity beset so delicate an investigation, at once become apparent. The physiology of such regions as the red nucleus, the posterior commissure, the hypothalamus, the palæo-striatum (globus pallidus, nucleus accumbens, area parolfactoria) and the neo-striatum (putamen and nucleus caudatus), is still a matter of conjecture. It can readily be understood how extremely difficult it is to produce sharply localized lesions in these regions. The formation of a thrombus may throw out of action a much larger area than is desired, and the direction or shape of the thrombus plays an important part. At the present time one cannot eliminate the element of chance from such experiments, but out of a series a few useful results may be obtained.

I now propose to discuss a series of sections prepared from the brains of a rabbit and a cat. The sections from the rabbit were prepared in the Central Brain Institute and were stained by the Weigert-Pal and van Gieson methods. The sections from the cat were stained by the Marchi method.

In both cases the posterior commissure was pierced by a needle (rabbit, fig. 9; cat, figs. 15 and 16) and the grey matter in front and on the mesial side of the red nucleus (region of the nucleus interstitialis)

was divided. In the cat the central grey matter of the aqueduct and the nuclei of the posterior commissure (Darkschewitchi) were also injured. The rolling movements which resulted in both cases appeared immediately after the operation, diminished after a few days, finally showing themselves only in a persistent tendency to fall towards and to lie on the normal side. Circus movements to the side of the lesion resulted only in the case of the cat and persisted for a few days only.

In the case of the rabbit, which survived for six months after operation, careful observation failed to discover any tendency to turn to one side more than another; it was highly probable, therefore, that Darkschewitchi's nucleus, which is associated with circus movements, escaped injury. Forced movements in the antero-posterior plane were seen in the cat only, and appeared as stepping and staggering movements. They were only present for the first few days after operation, and were probably due to lesion of the nuclei near the middle line.

The forced position of the eyes in both animals was that which usually accompanies the phenomenon of rolling movements to the right [5]. Both eyeballs were rotated round the visual axis towards the right side, the right eye being directed downwards, the left upwards.

It is interesting to note that both animals appeared to be blind immediately after operation, probably owing to the cross-section through the dorsal division of the posterior commissure. Later this passed off but hemianopsia towards the right persisted in both.

Microscopical examination of the brain and spinal cord of the cat showed the extent of the injury to be as follows.

The lesion in the middle line extended so far back that both bundles of Monakow were severed at their crossing, and they were consequently degenerated down to the lower segments of the cord. Both pyramidal tracts showed degeneration; the left was injured in the motor cortex as a result of the primary lesion, and also where the needle after piercing the midbrain reached the pes pedunculi.

The primary and secondary degenerations found in the posterior longitudinal bundles and the posterior commissure, with its nuclei and their connections, are particularly important. As these degenerations are for the most part identical in the rabbit and the cat, the fact that the Weigert-Pal and van Gieson methods were used in the one case and the Marchi method in the other makes the physiological and anatomical comparison of the two series more interesting.

Fig. 6.

Fig. 7.

Fig. 8.

Fig. 9.

Examination showed complete division of the posterior commissure. This is a lesion rarely described in literature, but was noted by Probst [13], Buzzard and Collier [2]. In the rabbit the secondary ascending vestibular tracts in the posterior longitudinal bundles were divided. In

Fig. 10.

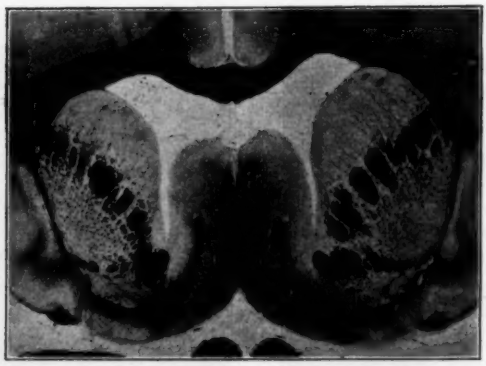

Fig. 11.

FIGS. 6-11.—Rabbit. Lesion of the commissural nuclei on the left side. Descending degeneration of the mesial part of the left posterior longitudinal bundle, and of the lateral horn of the right posterior longitudinal bundle. The left globus pallidus is diminished in size.

the cat the lesion was more limited to the middle line. It was found that on the left side (the side of the lesion) both the commissuro-medullaris and the interstitio-spinalis (Boyce's tract) tracts were degenerated

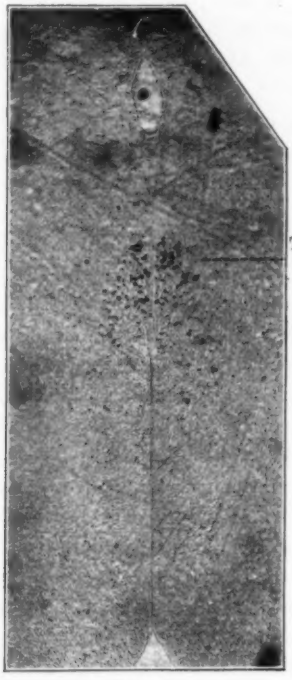

Fig. 12.

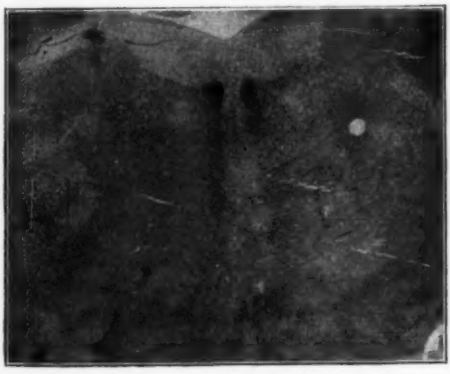

Fig. 13.

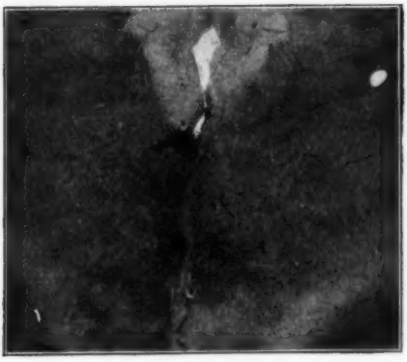

Fig. 14.

(figs. 12, 13). The lesion crossed the middle line, injuring the right posterior longitudinal bundle, and the interstitio-spinalis tract of this side also showed degeneration (fig. 14).

In the rabbit the left posterior longitudinal bundle in the medulla oblongata, particularly in its median portion, was less prominent than on the right side (fig. 6). In the pontine region this difference was less noticeable. It appears probable, therefore, that in this case the nucleus commissuræ posterioris suffered less injury, and as a result the commissuro-medullaris tract.

The most important point in these two experiments is that they afford an opportunity for seeing the orally situated structures with which the mesencephalic nuclei are connected.

In the rabbit, where rolling movements alone were seen, the lesion of the commissural structures was more limited. With the Weigert-Pal stain the corpus striatum presents the same picture as that described by Monakow in a rabbit [7]. These histological changes are as follows: The entire left globus pallidus, less so the putamen, but not the nucleus caudatus, show a decidedly atrophic appearance, compared with the normal side. Forel's field on the affected side is also rather thin, while the lamina medullaris externa thalami is not at all prominent (figs. 9, 10).

In the cat (241) the Marchi stain demonstrates the course of the striopetal fibres from the commissural nuclei. In following the fibres from the commissural region it is seen that the crus cerebelli ad thalamum of the left (side of lesion) is the more prominent; the majority of its fibres disappear orally in the neighbourhood of the lamina dorsalis thalami (fig. 16). From the capsule of the red nucleus a number of degenerated fibres pass at first ventrally, then laterally, in the direction of Forel's field. The lamina medullaris externa is thickly dotted with fine black spots (fig. 17). It is certain that a number of degenerated fibres are lost in the body of Luys's nucleus, in Forel's field, and probably also in the middle and anterior thalamic nuclei. The majority, however, of these ascending fibres, which are in all probability mostly vestibular, disappear in the direction of the globus pallidus (fig. 18). The external capsule of the putamen, especially in its anterior part, is markedly degenerated. In the putamen proper there is very little evidence of degenerated fibres. Fig. 18 shows the capsule on the right side, where, however, the degeneration is not nearly so great as on the left side, where the commissural nuclei are completely destroyed. It was impossible to obtain a satisfactory photograph of the left side.

Fig. 15.

Fig. 16.

Fig. 17.

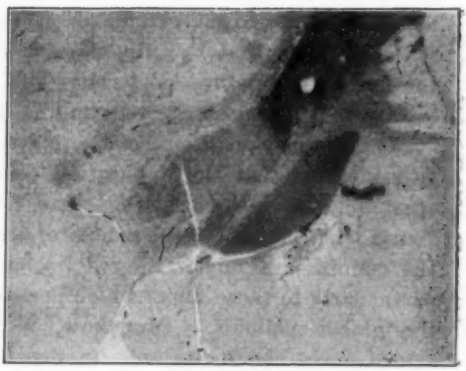

Fig. 18.

FIGS. 12-18. — Cat. Lesions of the commissural nuclei, mainly of the left side. Descending degeneration of the interstitio-spinal tracts, and less so of the commissuro spinal tracts. Ascending degeneration towards the globi pallidi, mainly on the left side.

These facts confirm results obtained by me in experimental work on cats. In some of these animals the globus pallidus itself was injured, or the lamina medullaris externa was severed. In such cases histological examination shows degeneration of fibres to the commissural nuclei and red nucleus on the one side, and to the globus pallidus on the other. Further, they agree with the anatomical observations of Wilson [23], who with the use of Clarke's apparatus demonstrated the existence of fibres passing from the putamen to the region of the globus pallidus and thence towards the capsule of the red nucleus.

I therefore conclude from this evidence that the commissural nuclei are in neuronal continuity with the globus pallidus of the same side. This connection consists of at least two neurons between the globus pallidus and the commissural nuclei, whereas in the reverse direction but one neuron exists.

These results may appear unexpected to the physiologist and the clinician, but if the work of Bechterew, Probst and Dejerine [3] is carefully considered, it is evident that considerable support for the results is forthcoming.

In the last section I called attention to the agreement in many points between my work and that of Wilson. In certain particulars, however, we differ. Wilson speaks of connections from the region of the globus pallidus passing to the region of the red nucleus. In all my experiments the red nuclei were intact, and it is extremely probable that the bulk of the globus pallidus connections do not reach the red nucleus at all, but pass to the two nuclei situated anteriorly and medially to it. It is probable that this investigator did not realize the existence of the nuclei commissuræ posterioris and interstitialis and their descending tracts in the posterior longitudinal bundle.

It is important when considering results obtained by other workers to remember that the application of the nomenclature differs somewhat in different countries. The English workers apply the term "ansa lenticularis" to the whole of the mass of fibres lying between the commissural nuclei, the red nuclei and corpus striatum, and more particularly to those fibres which penetrate the internal capsule to join the globus pallidus. Monakow, Winkler, Potter, Dejerine and his school apply the name only to the fibres lying between the mesencephalic nuclei and the more anteriorly situated parts of the corpus striatum.

It is not my intention to discuss afresh in detail the physiological points as applied to the human subject raised in this and in my earlier

paper [9] in which an anatomical-physiological investigation of the posterior longitudinal bundle revealed only two descending tracts in its median part. One passes down from the nucleus commissuræ posterioris (tractus commissuro-medullaris) and is associated with circus movement and conjugate deviation of the eyes to the same side; the second tract passes down from the nucleus interstitialis (tractus interstitio-spinalis, Boyce's tract) and is associated with rolling movement and the development of the Majendie-Hertwig squint. In this paper (p. 418) I concluded thus: "If this symptom (tendency to fall to the right) is present where the disease is localized cephalad to the posterior commissure, then from experimental findings the lesion is to be localized in the optic thalamus or striate body on the left side." When this was written I had already made use of the direction of these forced movements for purposes of localization in brain disease, particularly for diagnoses of frontal diseases.

It is interesting to find that in war literature is the first, and I think, decisive confirmation for this solution of the localization problem. Gerstmann [4], writing in 1916, published six cases of unilateral lesion of the frontal brain. In all the cases there was a disturbance of equilibrium demonstrated as a falling to the healthy side. The writer of the paper was evidently unaware of my paper (1914), and therefore could not appreciate the confirmation given to my suppositions. I therefore regard this falling to the healthy side as an important diagnostic sign in disease of the frontal lobe, or, to state it more exactly, of involvement of the globus pallidus or its connections with the commissural nuclei. Further experimental as well as clinical evidence seems to show that only in lesions of the globus pallidus do lasting circus movements and conjugate deviation of the eyes to the side of the lesion or a tendency to fall over to the healthy side result. From this one must admit continuity of anatomical connections from the vestibular region upward through the brain-stem to the globus pallidus. It must be remembered that a lesion of the putamen alone causes these disturbances for a short time only.

Section II.

Pathological lesions in man comparable to the above experimental lesions in cats and rabbits are rare.

In the Brain Institute in this city I found nothing to correspond with them. My attention, however, was drawn to a series of sections of the brain of a case of Meer en Berg, where a thrombotic process had caused atrophy of a great part of the left hemisphere.

The cortex of the entire frontal and parietal region was reduced to a thin lamella in which no traces of the convolutions could be detected. The corpus callosum was atrophied. The left lateral ventricle was enormously distended. Of the left corpus striatum the nucleus lentiformis was completely absent, and no part of the left putamen could be considered normal, and only a small number of cells were found in the globus pallidus. As this case has been discussed for other purposes and drawings of sections of it published [19], I shall limit myself to a statement of those details which are of importance for the present research.

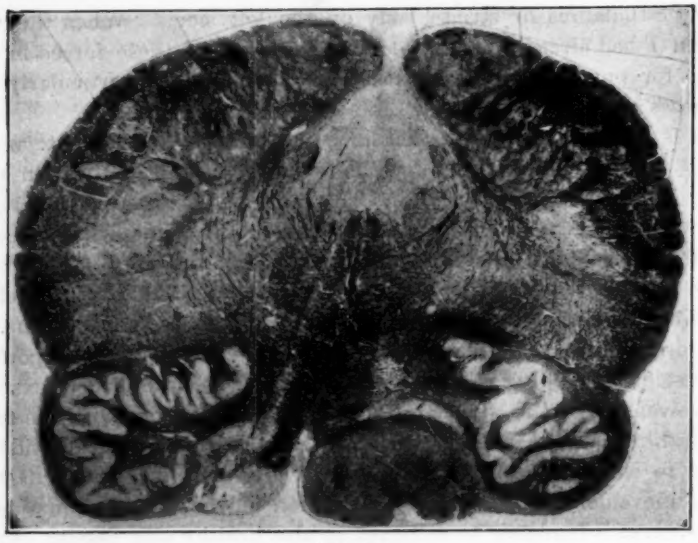

Fig. 19.

In the first place I would direct attention to the difference in size of the posterior longitudinal bundles, that on the side of the lesion being diminished (figs. 19, 20, 21, 22, 23). This difference in size must be explained by the interdependence of the globus pallidus and the homolateral nuclei (nucleus interstitialis and nucleus commissuræ posterioris), as has been shown experimentally in the rabbit. This being so, partial destruction of the globus pallidus is inevitably associated with atrophy of these nuclei and insufficient development of the homolateral fibres descending in the posterior longitudinal bundle [9].

The work of Edinger, Ramon y Cajal and my own unpublished observations on the constitution of the ventral part of the posterior commissure, would show that those nuclei receive afferent impulses from the heterolateral branch of the commissure, this being the continuation of

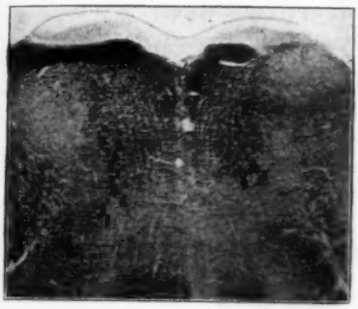

Fig. 20.

Fig. 21.

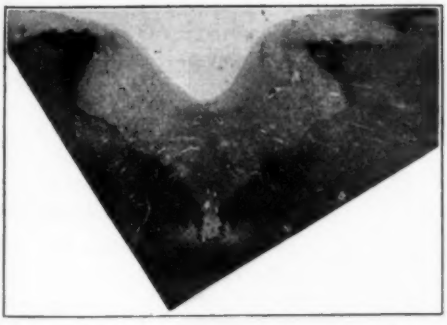

Fig. 22.
Note the fewer fibres in the mesial part of the left posterior longitudinal bundle.

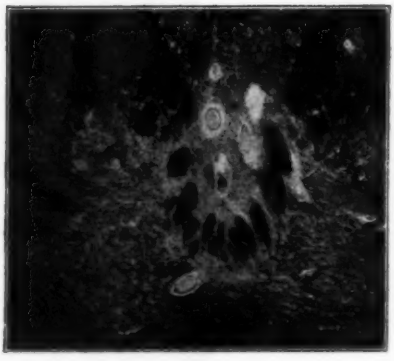

Fig. 23.
A portion of fig. 22 photographed under a higher magnification.

the lateral horn of the posterior longitudinal bundle. It is therefore not surprising to find in this case that the right arm of the commissure contained fewer fibres than the left (fig. 22).

This case is comparable with the experimental rabbit; in the rabbit

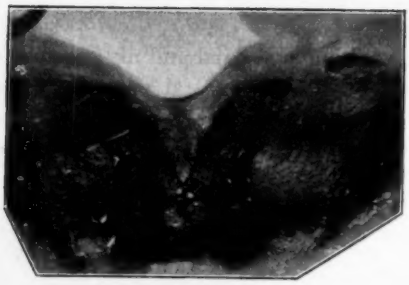

Fig. 24.

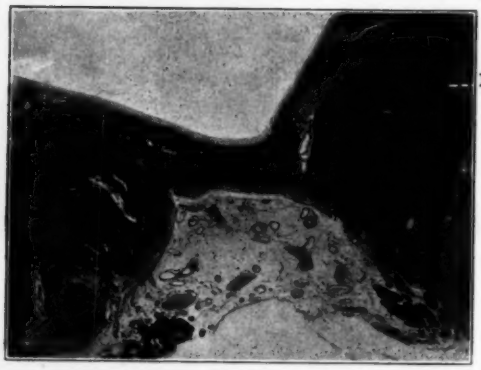

Fig. 25.

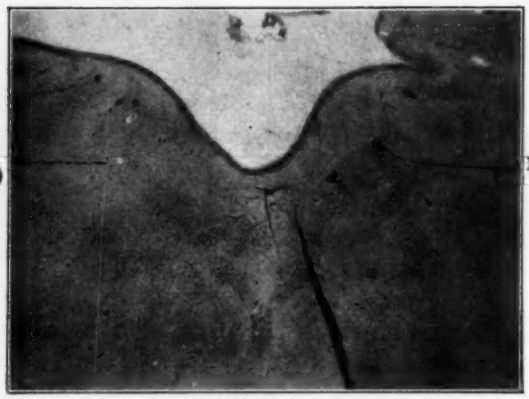

Fig. 26.

FIGS. 19-26.—Section of a human brain in which a destructive lesion of the left corpus striatum had occurred several years before death. The left nucleus commissuræ posterioris and nucleus interstitialis are atrophic. Poverty of fibres in the lateral horn of the right posterior longitudinal bundle, and in the corresponding part of the posterior commissure. In fig. 19 note the smallness of the left posterior longitudinal bundle owing to absence of the tr. interstitio-spinalis.

the lateral wing of the posterior longitudinal bundle on the side of the lesion involving the commissural nuclei was more voluminous than on the other side (fig. 6). In the human brain destruction of the left globus pallidus is also associated with a greater development of the lateral wing of the left posterior longitudinal bundle (fig. 21).

From these facts we must recognize a cerebropetal structural and functional continuity between the left corpus striatum, the right arm of the posterior commissure and the lateral wing of the right posterior longitudinal bundle. Further, it is also found that the left corpus striatum is cerebrofugally connected with the commissural nuclei, and by means of these with the descending fibres in the innermost part of the mesial segment of the left posterior longitudinal bundle.

Finally I would direct attention to the red nucleus.

When the series of sections are examined from below upwards it is found that these nuclei first appear in the same cross-section (fig. 24). It is probable, therefore, that the caudal parts at least of these nuclei are not dependent on the corpus striatum of the same or the other side.

In fig. 25 the frontal part of the right red nucleus is seen, but of the left there is no trace. It would, however, be premature to conclude that the frontal part of the red nucleus has a special relation to the homolateral corpus striatum, since the exact homology of those regions is unknown. The difference in the oral parts of the red nuclei might be due to the fact that in man the nucleus interstitialis is represented by the frontal part of the red nucleus.

From further experimental work I maintain the conclusions put forward in my former paper [9], that the nucleus commissuræ posterioris and the nucleus interstitialis represent superimposed vestibular nuclei. These nuclei receive their stimuli from the ascending elements of the crossed posterior longitudinal bundle via the posterior commissure. The descending fibres from them, the tractus commissuro-medullaris and the tractus interstitio-spinalis, are situated in the mesial division of the posterior longitudinal bundle. The descending fibres or tracts are concerned with locomotion in two planes (circus movement with conjugate deviation of head and eyes, and rolling movement with Hertwig-Majendie squint).

It must be admitted that for some reason a lesion of the ascending elements of this vestibulo-motor nerve chain prevails in its effects over lesions of the descending elements. This is shown by the fact that in a series of hemisections from the pons upwards the direction of the

forced movements changes as soon as the posterior commissure is reached. Further, the supra-nuclear centres are connected with the corpus striatum, or at least with the oral part of the globus pallidus. The direction of the forced movement does not change wherever the supra-nuclear section is made. If an animal with a lesion in this part survives sufficiently long some loss of fibres may be found in the mesial part of the posterior longitudinal bundle, and also in the wing of the posterior longitudinal bundle of the crossed side. This descending degeneration has been observed in the case of a patient of my own with recent destruction of the globus pallidus, and also in similar cases recorded by Dejerine and Roussy [16].

Section III.

My earlier work on this subject [9] indicated that the commissural nuclei (N. commissuræ posterioris and N. interstitialis) as well as the secondary, and perhaps tertiary, vestibular tracts which compose their afferent systems, are concerned exclusively with locomotion and conjugate deviation of the head and eyes in the horizontal and frontal planes. It is proposed to give here a short note on the fibres and nuclei which subserve forced movements in the sagittal plane, that is locomotion and conjugate deviation of the head and eyes upwards and downwards.

The nuclei and fibres which determine forced movements in the horizontal (circus movements) and frontal (rotation round the body axis) planes are situated symmetrically on either side of the middle line, one system co-ordinating the deviation or rotation to the right, the other to the left. Physiological and clinical data tend to show that entirely different nuclei and tracts determine vertical deviations. This is not surprising since the one set of movements—standing up, looking upwards, falling backwards, going backwards—is not the reflected image of the other set—stooping down, looking down, falling forward, going forward.

The upward and downward forced movements are never of the violent character seen in rabbits when the vestibular nerve has been injured. Further, they seem very easily compensated. During the first few days after operation on the cat (241) there was a tendency to recoil, to fall backward and to go backward, and a very slight pressure under the chin caused the animal to sit up. This form of forced movement in the sagittal plane invariably follows a lesion of the nucleus

tecti cerebelli in the cat and the pigeon. It is interesting to find that there is some clinical evidence on this point, similar forced movements occurring in cases of tumour of the cerebellum involving the nuclei tecti.

Wallenberg [22] working with pigeons found that after lesions of the superior cerebellar peduncle there was a tendency to retrogression, and thought that injury to some nucleus in this region was associated with the development of these movements. Marburg, Bing, and Ingvar also found that lesions of the spino-cerebellar tracts in animals were associated with disturbances of locomotion in the antero-posterior direction.

In 1907 I described the terminations of fibres of the vestibular nerve in the nucleus tecti. It seems highly probable that the nucleus tecti plays the same part in forced movement in the antero-posterior direction as Deiters' nucleus and the descending vestibular nucleus do in circus and rolling movements. The fact that the ventral and dorsal spino-cerebellar tracts terminate in the nuclei tecti seems to corroborate this view [10].

In a series of sections through the brain of the cat (241), already referred to, a tract of degenerated fibres is seen on both sides of the section lying on the inner side of the anterior cerebellar peduncle (fig. 13). The position of this tract is almost identical with the hook-like structure found by Russell [16] in dogs after a median incision between the nuclei tecti. This structure was also described by Thomas [18]. The difference between my case and the cases of Russell and Thomas is that in their cases the degeneration was cerebello-fugal while in mine it is cerebello-petal. This in no way serves as an argument against my view but is rather evidence in favour of it, since from the time of Held [5], who first drew attention to the fact, it has been more and more appreciated how frequently the ascending and descending secondary and tertiary vestibular pathways lie in the same areas.

At present we can only surmise which supra-mesencephalic nucleus receives these fibres, but probably it is situated ventrally to the posterior longitudinal bundle in or near the raphé. This suggestion is made from a study of the rabbit already described where the structures of the median line were intact, and where no trace of forced movements in the vertical plane occurred.

Physiological and clinical observations therefore tend to show that a lesion near the median line in the thalamic region will cause

staggering, and walking or falling backward, as do lesions of the prosencephalon if not situated too ventrally.

It seems justifiable to assume ascending connections similar to the tertiary striatal connections of the commissural nuclei, but passing to the palæostriatal nuclei septi.

Although experience has shown the utility of the physiological-anatomical method it must be understood that great care is necessary in its application. This is particularly so in attempting to demonstrate the tertiary vestibular connections where conclusions have to be drawn from transient and puzzling forced movements in the antero-posterior or sagittal plane. The forced movements in this plane are never violent even after lesions of the primary connections. It is also important to remember that the forced movements in the other planes (circus movement and rolling) decrease in strength the farther the lesion is from the primary vestibular fibres.

I may say in conclusion that I have carried out certain experiments and collected some clinical data on the position of the vestibular nuclei, the superimposed nuclei and their connections which may excite forced movements in the sagittal plane in the opposite direction to those already described, i.e., falling forward and locomotion forward. There is some evidence that the nucleus ventralis raphé is associated with this type of movement. In one experiment where the lesion involved the basal longitudinal bundle (Wallenberg) near its origin in the frontal brain the animal never sat up again in a natural manner, but held its head down. It may be surmised that the secondary tracts run up near the raphé and are situated somewhat ventrally. Further it seems probable that the tertiary ascending and descending fibres dealing therewith are to be found in the area of the basal longitudinal bundle of Wallenberg.

Summary and Conclusions.

(1) Persisting circus movements and lateral conjugate deviation of the head and eyes to the affected side, and a tendency to fall to the normal side after cerebral lesions, is due to injury of the oral part of the globus pallidus, or of its connections with the commissural nuclei (nucleus commissuræ posterioris and nucleus interstitialis). Hence the conclusion seems warranted that the tertiary vestibular tracts, lesions of which produce the same symptoms, terminate in this palæostriate centre.

The secondary vestibular tracts which ascend in the posterior longitudinal bundles cross the middle line by way of the posterior commissure before entering the nucleus commissuræ posterioris and nucleus interstitialis. In the diagram in my earlier paper [9] these ascending vestibular tracts were wrongly indicated as terminating in the commissural nuclei before crossing the middle line.

(2) It has not been possible to determine by the anatomical-physiological method the chains of neurons concerned in forced movements in the sagittal plane, i.e., recoil, retrogression, conjugate deviation of the head and eyes upwards; falling forwards and deviation of the eyes downwards. Experiments on cats, in which lesions of the nucleus tecti and of the superior cerebellar peduncle produce a tendency to recoil, recall the experiments on pigeons by Wallenberg, who assumed the existence of some such centre in or near to the superior cerebellar peduncle. Clinical and physiological observations lead us to suppose that structures exist in the mesencephalon, near the raphé and ventral to the posterior longitudinal bundle, lesions of which cause falling backwards and deviation of the eyes upwards. There is also experimental evidence that lesions of the palæo-striate nucleus septi (Kappers, de Vries) cause recoil and retrogression.

Near the middle line but more ventrally situated there are structures (? the basal longitudinal bundle of Bischoff and Edinger), lesions of which produce a tendency to fall forwards and deviation of the eyes downwards.

I have to acknowledge my indebtedness to Dr. Ariëns Kappers and Dr. Brouwer for their permission to make use of the material of the Central Brain Institute in Amsterdam, and to Mrs. Shaw Dunn for her kind help in correcting the English of this paper.

REFERENCES.

[1] Bechterew. *Pflüger's Archiv*, 1884, **34**, 362.
[2] Collier and Buzzard. *Brain*, 1901, **24**, 177.
[3] Dejerine. "Anatomie des centres nerveuses," 1901, t. 2, 405.
[4] Gerstmann. *Monatschr. für Psychiat. und Neurol.*, 1916, **40**, 6.
[5] Held. *Arch. f. Anat. u. Physiol.*, 1893, Anat. Abth., 201.
[6] Ingvar. *Folia Neurobiologica*, 1917-19, **11**, 205.
[7] von Monakow. *Gehirn pathologie*, 1905, IIte Aufl., 134.
[8] Muskens. *Psychiat. en Neurol. Bladen*, 1906, **10**, 64.
[9] *Idem*. *Brain*, 1913-14, **36**, 352-426.
[10] *Idem*. *Koninklijke Akademie van Wetenschappen te A'dam*, 1902, Deel 3, p. 4.
[11] *Idem*. *Nederl. Tijdschrift voor Geneeskunde*, 1918, **1**, 1272.
[12] Prévost. "Deviation conjugée," *Thèse de Paris*, 1868, p. 129.
[13] Probst. *Monatschr. für Psychiat. und Neurol.*, Blz. V., 1905, **17**, 1.

[14] PRUS. *Wiener Klinische Wochenschr.*, 1899, **12**, 1199.
[15] ROUSSY. "La couche optique," *Thèse de Paris*, 1907, p. 175.
[16] RUSSELL. *Phil. Trans. Roy. Soc.*, Lond., 1894, B, **185**, 837.
[17] SACHS. *Brain*, 1909, **32**, 180.
[18] THOMAS. "Le Cervelet," Steinheil, Paris, 1897, p. 95.
[19] VAN VALKENBURG. *Psychiat. en Neurol. Bladen*, 1911, **15**, 374.
[20] DE VILLAVERDE. *Trabajos del Laboratorie de investigationes biologicas de Madrid*, 1921, **18**, 161.
[21] VOGT, C. and O. *Sitzungsberichte der Heidelberger Akademie der Wissenschaften*, 1919. Abt. B, 14.
[22] WALLENBERG. *Anatomischer Anzeiger*, 1904, **24**, 142.
[23] WILSON. *Brain*, 1913-14, **36**, 427.

Proceedings of the Section of Neurology of the Royal Society of Medicine.

CLINICAL MEETING, NOVEMBER 9, 1922.

Dr. WILFRED HARRIS, President, in the Chair.

(1) *A Case of Tremor of Rare Nature.*

By Dr. ANTHONY FEILING.

Gladys C., aged 10½, was brought to the hospital on account of involuntary movements of the left side of the body. She was a full-time child, a breech presentation and at birth had white asphyxia. Sat at 18 months, walked at 3 years. Has never had fits or other illnesses, except measles.

At the age of 9 months involuntary movements were noticed on the left side of the body, and weakness in holding up the head. During the last six months these movements have become worse and have extended to the other side of the body. At times her voice is very feeble. No history of any nervous disease in the family. The child is well grown and appears quite intelligent.

There is a slight weakness of the lower part of the right side of the face, while the tongue is deviated slightly to the left. The left arm is the seat of a rhythmical tremor, more marked in the proximal parts of the limb. The movements produce rotation of the arm at the shoulder, pronation and supination of the forearm, and flexion and extension of the fingers. The rate is about two to the second. Both arms are hypotonic.

Similar movements affect the trunk and the legs, though to a less extent. In the legs also the proximal muscles are involved to a greater extent than the distal. There is no actual paralysis, though the power of the left arm and leg is less than in the right limbs. The deep reflexes are present and the plantar responses are flexor.

(2) *Parkinsonian Syndrome associated with Right Hemiplegia, showing Peculiar Disturbances of Tone and Posture in the Limbs on the Hemiplegic Side.*

By Dr. DOUGLAS MCALPINE.

Patient, a female, aged 20, was quite well until April 18, 1919, when she developed a typical attack of encephalitis lethargica, complicated from the outset by a right hemiplegia. Her present condition developed gradually within a few months from onset.

The following is a brief summary of her present condition :—

Parkinsonian facies, smile and speech, with slight right hemiplegia and definite extensor response on right side; on left side doubtful extensor response. Power quite good all four limbs; no sensory disturbances.

At the proximal joints in all four limbs there is a slight resistance to both flexion and extension by passive movements, most marked in the lower limbs. If the fingers or wrist of the right hand be passively moved into any position, such position is maintained involuntarily. Right ankle when inverted or everted remains in that position; this is not seen however in dorsal or plantar flexion at proximal joints, nor in the limbs on the left side.

Voluntary movements.—Extension at elbow is possible only when fingers are extended: with the fingers flexed there is always accompanying pronation; extension of fingers is possible only when patient voluntarily abducts the arm, flexes the elbow, pronates the forearm and flexes wrist, or when she extends the hyperpronated elbow. The postures of hand and wrist on voluntary movement of the limb tend to take one of four patterns :—

(1) Flexion of fingers and wrist. (2) Extension of fingers and thumb, wrist being flexed or slightly extended. (3) Extension of wrist and first phalanges, with flexion at interphalangeal joint and apposition of thumb. (4) Same position of fingers as in (2), but with flexion of the wrist and pronation of the forearm. The position of the elbow is variable.

All voluntary movements of the hand are carried out slowly and with difficulty. The phenomenon of tonic innervation is well seen in the right hand and wrist. If patient when grasping the observer's hand is then told to relax her grip she is unable to do so for a period varying between fifteen seconds and two minutes; she has to manœuvre her arm into the position described as necessary when extending the hand. This condition is not seen at the proximal joints, but occurs to a slight extent at the right ankle. There are no athetotic movements, nor motor apraxia. A flexion and sometimes an extension reflex (as described by Riddoch and Buzzard) is obtainable in both upper limbs when a nocuous stimulus is applied to either extensor or flexor aspect of arm.

On assuming the upright posture the right arm at once becomes extended at elbow, hyperpronated, flexed at wrist and deviated to the ulnar side, with fingers flexed into palm. As soon as right foot touches the ground it becomes powerfully inverted, with plantar flexion of foot and toes, but the hallux is dorsiflexed so that the pad of the toes alone touches the ground; at the same time there is extension of the knee. After half a minute or so the tonic spasm of the foot gradually relaxes and the right foot assumes its correct posture on the ground. On attempting to walk the right leg is overflexed at the hip and the whole leg goes into extensor spasm again, the attitude of the leg at this stage resembling that depicted in the goose-step of the German soldier. Gradually the right leg is lowered and toes approach the ground; then, as spasm relaxes, the heel is gradually lowered until it touches the ground, the weight meanwhile being transferred to right leg. As the right leg is carried forward the right arm, maintaining the posture described above with

palm turned outward, is powerfully retracted and abducted at shoulder, and as the patient transfers her weight on to the right leg the right arm comes forward again into line with the body.

Remarks.—In this case there is evidence of a moderately well developed condition of Parkinsonian rigidity associated with a slight right hemiplegia, and in all probability with some disturbance of the left pyramidal tract, as evidenced by the nature of this plantar response and the presence of a well-marked flexion reflex in the left upper limb; despite this bilateral pyramidal involvement there is an entire absence of pseudo-bulbar symptoms. There is no evidence that the phenomenon of tonic innervation depends on a lesion on a higher plane than the internal capsule, which however was the case in seven out of the nine cases collected by Wilson and Walshe. The condition seems to indicate lack of reciprocal inhibition of antagonists, so that one muscle group remains contracted despite volitional attempts to innervate the opposing group of muscles. In this case apparently the same phenomenon is present both on voluntary and on passive movement, and in the maintenance of a posture of right hand brought about by the observer; therefore no separation is possible between the phenomena occurring on voluntary and involuntary movement. It seems certain that in this case the condition of tonic innervation can be explained by a central lesion resulting in a disturbance of reflex tonus. The posture which develops in the limbs on the right side on standing or attempting to walk is clearly determined by the assumption of the upright position, and resembles closely the antigravity posture as described by Sherrington in the decerebrate animal.

I am indebted to Dr. Campbell Thomson for permission to show this case.

Dr. RIDDOCH, referring to the flexion reflexes of the upper limbs, said they were similar to those observed by Buzzard and himself in hemiplegia due to cerebral and spinal lesions. In this case there can be no doubt of the existence of a right-sided hemiplegia, and there is evidence that the left pyramidal tract has suffered too, in the indefinite type of the plantar reflex on this side. The tonic state of the muscles on the right side of the body, the "lead-pipe rigidity" of the limbs, and the persistent maintenance of postures, differs from that seen in both paralysis agitans and post-encephalitic lesions. The rigidity suggests that it might be the result of a combined hemiplegic hypertonicity and Parkinsonian rigidity. The postures of both the upper and lower limbs are not those usually observed in simple lesions of the pyramidal system. He emphasized the remarkable feature that the patient can open her hand only on supinating the arm, and that the whole limb extends when she closes her fingers. Similarly in advancing the leg the whole limb extends, and the ankle dorsiflexes only a considerable time later.

The PRESIDENT asked whether the present symptoms were the immediate sequel to the attack of encephalitis, or whether they had been progressive.

Dr. MCALPINE replying said that there was no interval between the acute symptoms of encephalitis and the symptoms which the patient now presents; these have been progressive. He was unable to accept Dr. Riddoch's suggestion

that the hypertonicity is due to the association of a hemiplegic and Parkinsonian rigidity.

(3) *A Form of Juvenile Amaurotic Idiocy.*

By Dr. GEORGE RIDDOCH.

The patient, aged 10, was the child of Jewish parents, who were also first cousins. A brother aged 13, and a sister aged 8, are both alive and well. Birth was normal and the child was breast-fed until 18 months of age. He walked at 9 months and used simple words at 1 year. Development was normal until 4 years of age when the legs became weak. At 6 the upper limbs were also affected and obvious symptoms of mental deterioration set in, the child becoming dull and apathetic, with occasional outbursts of screaming and destructiveness. At the age of 8 years vision was noticed to be affected, and a year later there was complete paralysis of all limbs, curious myoclonic movements, over-reaction to loud noises, blindness and complete idiocy. The child also became subject to epileptiform fits. Any loud noise was liable to evoke irregular purposeless movements. The child has wasted considerably.

Present condition.—Complete dementia, blindness and spastic paralysis of upper limbs in flexion and lower limbs in extension. Lies on his back with head to one side and saliva dribbling from his open mouth. Quick involuntary movements, especially of upper limbs, occur frequently. These myoclonic movements can be evoked by the slightest tap on any part of the body, and sometimes by a loud noise. They are often bilateral and symmetrical and are then accompanied by movements of the head and face, contraction of the muscles of the trunk and a grunting noise. All tendon reflexes are much increased and the plantar response is extensor on both sides.

Ophthalmoscopic examination reveals advanced optic atrophy and much pigmentary degeneration of the retina; there is a large mass of pigmentary change near the left macula. No cherry-red spot at the macula. The Wassermann reaction of the blood was reported as being doubtfully positive.

He discussed the relation of this case to the Waren Tay-Sachs type of amaurotic family idiocy, which is limited to the Jewish race, and to the juvenile forms of this disease which have been described by Batten and Mayou and by others.

The PRESIDENT said he had found it difficult to get a satisfactory view of the fundi, but that such changes as he had seen resembled those of retinitis pigmentosa.

Dr. GORDON HOLMES pointed out that this case differs in many of its present symptoms from the typical cases of infantile and of juvenile amaurotic idiocy. The term idiocy should not, in fact, be applied to such cases, since the mental state of the patient was apparently normal till 5 or 6 years of age. The most striking difference from the Spielmeyer and Batten-Mayou groups is that in this patient there are, in addition to optic and retinal atrophy, large irregular patches of pigment in the retinæ which resemble those due to

syphilitic retino-choroiditis. He was consequently not surprised that on one occasion the Wassermann reaction was positive or doubtful. Further, the pigmentary changes are grosser and more widely scattered over the fundus than in the Batten-Mayou group. In many of these cases the retinal degeneration belongs to, or resembles, the retinitis pigmentosa type, but the fundus changes he saw were not characteristic of this condition. There were unquestionably many forms of progressive dementia and paralysis associated with retinal degeneration, each rigidly typical for the several numbers of the family it affects, but differing in many respects from family to family.

Dr. PARKES WEBER suggested the possibility that the condition was one of juvenile general paralysis; the same type of spasmodic movements is not uncommon in this disease, and similar fundus changes are occasionally met with.

Dr. FEILING had also observed similar ocular changes in syphilitic conditions; he had recently seen them in a patient with tabes dorsalis.

Dr. RIDDOCH in replying admitted that the symptoms differed in many respects from those seen in the Batten-Mayou and Spielmeyer groups, and he must admit that similar retinal changes are found in both retinitis pigmentosa and in syphilitic conditions, but he could not see any justification for the suggestion that his case may be merely one of juvenile general paralysis.

(4) *A Specimen showing Endothelioma Cerebri in an Unusual Situation.*

By Dr. J. P. MARTIN.

Patient was admitted to the National Hospital under the care of Dr. Taylor, April 18, 1922, and died May 20. For three years he suffered with pins and needles in the third, fourth and fifth fingers of the left hand; this feeling was not present constantly and usually occurred in the morning. It spread slowly up the left arm, and he became unable to grasp objects with the left hand. Towards the end of 1920 the right arm was affected in the same way, but in it the paræsthesiæ spread from above downwards.

In January, 1921, he was admitted to St. Thomas's Hospital; his legs had been shaky but were still strong and did not cause any disability in walking; after lying in bed for four days he became completely paralysed. He gradually improved and was discharged three months later.

About July, 1921, he began to suffer from attacks of breathlessness. He was re-admitted to hospital, and again became weaker while lying in bed. About October, 1921, he became unable to feed himself or to use his arms. He never had dysuria or pain. On about a dozen occasions in three months before his admission to the National Hospital he had seen double.

On admission very helpless, with cyanosis of face and lips, and occasional attacks of breathlessness. A few nystagmoid jerks developed on extreme deviation of the eyes to either side, and there was slight left facial weakness.

There was nowhere loss to painful, tactile or thermal stimuli, but the appreciation of vibration was absent in both arms and both legs. The sense

of position was lost in the right hand and arm and in both feet, and impaired in the left hand. There was complete astereognosis.

Patient could not raise his head from the pillow, but could turn it from side to side. When he was sitting in a chair his head fell forwards. Both upper limbs were quite powerless, they lay slightly flexed at the elbows and wrists, with the fingers half flexed. There was no spasticity and no wasting or fibrillation of the muscles. The lower limbs lay at rest in full extension. The amount of power varied from time to time: after he had been lying down he was usually unable to make any movement, but after sitting up for a time he could make movements of fair power at all joints.

All the arm-jerks were brisk, the knee-jerks exaggerated, ankle-jerks present with clonus, the abdominal reflexes absent, and the plantar responses both extensor. There was defective control over both anal and vesical sphincters.

The Wassermann reaction was negative, and the electrical reactions of the muscles were normal. X-rays showed no spinal lesion.

Patient died of hypostatic pneumonia.

Autopsy.—The tumour, which weighs 32·5 grm., is pear-shaped and firm in consistence. It fills and distends the cisterna magna, lying between the arachnoid and the pia mater. A small knob on its upper and posterior surface compresses the right lobe of the cerebellum. It lies against the foramen of Magendie, but has caused little hydrocephalus as the foramina of Luschka are unusually wide. The posterior surface of the medulla, from the tip of the calamus scriptorius downwards, is hollowed out by its pressure. The pressure affects particularly the cuneate and gracile nuclei, the restiform bodies being only compressed at their posterior borders. At the lower end of the medulla the tumour passes to the right of the mid-line so that the right dorso-lateral surface of the first cervical segment is compressed. The cord at this level is softened. Microscopical sections show the tumour to be a typical fibrous meningeal endothelioma.

(5) *Case of Sclerodermia.*

By Dr. MARTIN.

In March 1921, patient had an illness said to be influenza. In May she had difficulty in kneeling on account of pain in the thighs and back. In November she began to experience stiffness after standing for a short time. Menstrual periods have been irregular since January 1921. She has become thinner; a year and a half ago she weighed 8 st., now she weighs a little over 6 st.

Present condition.—High complexion, skin and subcutaneous tissues of the cheeks feel tough, skin of the nose red and shiny, lips puckered, mouth can be opened to a limited extent only. Scarcity of fat all over the body. The skin of the hands is hard, shiny and difficult to pinch up; the fingers are short, podgy and swollen, and cyanosed at the proximal phalangeal joints; their move-

ments are limited and in the little fingers there are flexor contractures. The feet are flat, the joints are swollen and the toes and forepart of each foot are cyanosed. The elbows cannot be fully extended, the knees are prominent and rounded, and full extension is not possible at them.

No changes are present in the nervous, circulatory or respiratory systems.

(6) *A Case of Dermatomyositis.*

By Dr. MARTIN.

The symptoms had commenced gradually one and a half years before with pains in the limbs and swelling in the hands and feet. There had been no rise of temperature during the time the patient had been under observation. The most striking feature was the marked hardening of the skin and the subcutaneous tissues, and the presence of firm nodules scattered irregularly over the limbs; one of these was excised. At this operation there was found to be a marked thickening of the subcutaneous tissues. The nodule consisted merely of a fatty centre surrounded by a capsule of dense fibrous tissue, in which there were numerous inflammatory cells. In this case the limbs only were affected.

Dr. PARKES WEBER, in discussing the second case, pointed out that dermatomyositis is an acute inflammatory lesion of the muscles which has been frequently confused with trichinosis in countries where this disease exists. On examining this case he found no evidence of an inflammatory lesion of the muscles, while it appeared to him that the nodules were merely circumscribed lipomata. The condition is therefore not a dermato-myositis, but an affection closely allied to sclerodermia.

The first case seems to be one of typical generalized sclerodermia. It was interesting that so much improvement had been noticed, and he inquired as to the treatment which had been adopted.

The PRESIDENT drew attention to the curious course run by some of these cases, and to the fact that the muscles are sometimes involved. He recalled a case of acute sclerodermia, from the manifestations of which the patient had made a complete recovery, but then developed typical symptoms of progressive muscular atrophy.

Dr. MARTIN in replying stated that the second case had been treated by thyroid extract, sinusoidal current baths and massage during the past three months, and that it was under this treatment that some degree of recovery had taken place.

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CLINICAL MEETING AT THE NATIONAL HOSPITAL FOR THE PARALYSED AND EPILEPTIC, QUEEN SQUARE, W.C., ON THURSDAY, JANUARY 11.

Dr. WILFRED HARRIS, President, in the Chair.

(1) *Case of Dystrophia Myotonica.*

By Dr. W. J. ADIE.

W. A., aged 44. Married. Enjoyed good health until March, 1917, when whilst undergoing military training he passed through a severe feverish illness diagnosed as influenza; during convalescence he suffered from severe pains in the lower limbs; the pains subsided in a few months but left behind them a weakness of the lower limbs which steadily increased, and soon appeared in the arms as well. About a year after the onset of weakness in the legs, and some time after the arms became weak, he noticed that he had difficulty in relaxing his grasp; this trouble persists. His facial appearance has altered considerably; all his muscles have wasted; his speech is not so clear as it used to be; his hair is falling out rapidly; he has lost over 2 st. in weight; he has not had sexual connection for some years and desire is absent. Apart from weakness in the limbs he feels well. He has never heard of a similar complaint or of cataract in any other member of his family. He has four healthy children.

Present condition: Facies myopathica; atrophy of sternomastoids, deep neck muscles, forearms and legs. Active myotonia in hand grasps. Reactive myotonia in tongue, small muscles of hands, deltoids and thighs. All tendon reflexes absent. Frontal baldness, acro-cyanosis, small soft testicles, narrow, high-arched palate.

(2) *Case of Myotonia Congenita.*

By Dr. LEWIS R. YEALLAND.

P. S., aged 18, male; one of twins. A paternal uncle suffers from cataract; nothing else from an hereditary point of view is discoverable. The patient was breast-fed and there was no difficulty in feeding him. He began to walk at the age of 2 years (a year later than his twin brother), was clumsy and made slow progress. At the age of 2½ his mother first noticed that when the patient's face was slapped for punishment, "his nose drew over to one side and remained there for a few seconds." At the age of 3, the patient was taken to India with his parents, and during his five years there nothing abnormal was observed; he walked normally and played games with other children. At the age of 8, he returned to England and began school. During his first week there (*a*) he saw double when looking at the blackboard from an angle; (*b*) his hand became "stiff" when writing and he was unable to release his pencil from it; (*c*) at the first school drill he was compelled to fall

out after twenty minutes' participation, on account of a gradually increasing stiffness which began in the neck and spread rapidly to the arms, trunk and legs. The stiffness was superseded by limpness, and in less than thirty seconds from the commencement of the symptoms he fell and was unable to move. He was taken home and remained in bed three days limp and helpless, but was able to swallow his food when fed. Similar attacks have occurred since during exertion, and an attack will come on after thirty minutes to one hour's walk in the cold. In warm weather he is almost free from the attacks. After prolonged rest the patient is much better, and he is in his best state the first thing in the morning after a prolonged rest. The condition is gradually becoming worse.

The patient is well developed. There are no deformities. Skin, mucous membrane, skull and spine, heart and lungs are all normal. The optic discs are clear and there are no evidences of organic changes in the central nervous system.

Repetition of any voluntary movement to order (e.g., eye movements, whistling, biting, yawning, flexion and extension of the elbow, wrist, knee or ankle) produces a gradually increasing tonic contraction of the part and will, if persevered in, result in complete cessation of movement. The same state of stiffness can be induced by the patient at will by throwing groups of muscles forcibly into contraction. Relaxation of muscles occurs gradually and is independent of the patient's will. Relaxation of the hand grasp is slow and awkward, the index finger extends first, followed by the others in succession, and the movement seems to be dependent on the patient's effort. A slow tonic contraction of muscles follows a sharp tap of the percussion hammer. The myotonic electrical reactions are positive.

Discussion.

Dr. James Collier considered that there was no doubt about the diagnosis of myotonia congenita in this case. It showed in a typical manner the effect of cold in increasing the tendency to myotonia, and resembled most reported cases in that the spasms were not decreased by exercise of the affected muscles.

The President asked Dr. Yealland if he had seen attacks in which the patient was helpless. Was it possible that these attacks were in any way similar to attacks of family periodic paralysis ?

Dr. Yealland replied that he had not himself observed such attacks, but the evidence he had been able to collect tended against this suggestion.

(3, 4, 5) *Three Cases showing Retraction of the Eyelids.*

By Dr. James Collier.

(3) *Case of Tumour affecting the Mid-Brain.*

The patient presents the following signs: Pronounced psychic impairment. Papillœdema. The pupils react very poorly to light, often the right pupil does not react to light at all. Retraction of both upper eyelids. Defective upward

movement of the eyes. Right facial weakness, especially on emotional movement. Absolute incontinence of urine. Slight weakness of the right side of the body, with extensor plantar reflex on that side.

(4) *Case of Mid-Brain Lesion.*

A. K. History: In October, 1921, the patient noticed shaking of the right hand; it passed off after about a fortnight. In February, 1922, the tremor returned: both the right arm and the right leg began to shake and she had double vision; her speech became slow and jerky.

Examination: Discs clear. Nystagmus: Vertical in right eye, oblique in left. Defective upper movement of both eyes; left eye turned slightly downwards and inwards. Ptosis of right upper lid; retraction of left upper lid with positive von Graefe's sign. Speech very ataxic. During speech there is a rhythmical upward and downward movement of the eyebrows and tremor of the head. There is a coarse tremor of the right hand. No loss of power in the limbs. No changes in the reflexes, except that the plantar reflex on the left side is doubtful.

(5) *Case of Disseminated Sclerosis with Retraction of the Eyelids.*

G. L., aged 41. Right leg began to drag seven years ago; since then symptoms have been steadily progressive, and consist of stiffness in both legs, spasms of lower limbs at night, precipitancy of micturition and incontinence.

Examination: Pupils equal; react normally. Nystagmus. Retracted lids, von Graefe's sign present. Slight intention tremor in hands; no ataxy or loss of power of upper limbs. Lower limbs very spastic, frequent flexion spasms.

Reflexes: Arm jerks all present; knee and ankle jerks exaggerated. Abdominal reflexes absent, plantar reflexes both extensor. Cerebrospinal fluid shows no abnormality.

(6) *Case of "Spondylose rhizomélique."*

By Dr. JAMES COLLIER.

The vertebral column is rigidly ankylosed throughout its length; the hip joints and knee-joints are also immobile; the right shoulder-joint shows great limitation of movement. The disease began ten years ago; patient has been in a spinal carriage for five years.

X-rays showed ossification of the short intervertebral ligaments.

DISCUSSION.

Dr. J. G. GREENFIELD asked whether there was in this case any sign of gonorrhœa, or of any focus of chronic sepsis. Some cases of this affection had been attributed by French writers to gonorrhœa. He remembered a case under Dr. Batten's care in the National Hospital in 1911,[1] in which gonorrhœa

[1] Case shown at Meeting of Neurological Section of the Royal Society of Medicine, May 4, 1911.

was suspected but could not be proved. In the majority of cases the disease commenced about the age of 20, and this fact, as well as the nature of the pathological changes and the distribution of the ankylosis (which always left the hands unaffected) distinguished spondylose rhizomélique from the chronic rheumatic diseases of the spine.

Dr. COLLIER replied that of six cases of this condition which he had observed none had suffered from gonorrhœa, nor was there any history or evidence of it in the present case. In one of his cases the disease came on after puerperal sepsis, but in the others there was no focus of infection. In the majority of his cases the spine had been ventrally curved, but in one it was curved backwards as in the present case. In one case the affection started in the neck, and in six months spread down the spine to the sacrum rendering the patient as helpless as if he had developed total paraplegia. He considered that the ankylosis of the spine was never bony as there was always pain on any attempts at passive movement.

(7) *Case of Disseminated Sclerosis with Muscular Wasting.*

By Dr. JAMES TAYLOR, C.B.E.

H. C., aged 47. Previous health good. Fracture of left leg below knee when aged 13. Present trouble started eight years ago by the left knee giving way and the left leg becoming weak. One year ago he discovered that on reading he "was using the left eye only." About the same date the left grasp became weak and a sensation of pins and needles was felt in the left forearm and hand. There was also dysuria.

On admission, November 6, 1922: Vision of right eye $\frac{6}{18}$, of left $\frac{6}{60}$. Left disc distinctly pale, chiefly in temporal half. Nystagmus on lateral deviation to both sides. Marked spasticity of left upper and lower extremities. Wasting of left trapezius and muscles of left shoulder-girdle. Weakness of right rhomboids. The left arm and leg are less bulky and thinner than the right. Subjective sensation of pins and needles in left forearm and hand, and numb feeling in the feet. Slight diminution to cotton wool and pin-prick over left leg. Extensors wasted. Plantars, right extensor, left flexor. Left ankle clonus. Knee and ankle jerks increased. Abdominals absent left, doubtful right. Wassermann reaction negative in blood and cerebrospinal fluid. X-ray examination shows lipping and osteophytic outgrowths of cervical and lumbar vertebræ.

The evidence of disseminated sclerosis in this case rested chiefly on the nystagmus, the difficulty in articulation and the signs of lateral sclerosis. The winging of the scapulæ was probably due to some other cause, and it was possible that the osteophytic growths in the spine might account for this and some of the other symptoms.

DISCUSSION.

Dr. COLLIER said that he would never admit wasting of muscles as a symptom of disseminated sclerosis.

The PRESIDENT said that he had seen quite definite atrophy of the interosseous muscles of the hands in disseminated sclerosis.

(8) *Case for Diagnosis: Spinal Compression or Disseminated Sclerosis.*

By Dr. F. M. R. WALSHE.

E. W., aged 37. Past health good. Patient has six children, all in good health. Duration of symptoms eighteen months. Onset with pain in sole of left foot, followed by stiffness at back of left knee. In three months time lost the use of left leg. Sensation of pins and needles in left leg when it was accidentally bumped. The right leg became weak and powerless two months later. Dysuria for the last six months.

On examination, December 27, 1922: No abnormality of the cranial nerves or upper extremities. Legs usually in rigid extension, feet plantar flexed, halluces in extension. Marked adductor spasm. Flexor spasms of the legs have been becoming more frequent. No sensory changes. Knee and ankle jerks increased. Plantars give extensor responses. Abdominal reflexes: Upper feeble, lower absent. Reflex responses to cutaneous stimulation of both legs very active. Cerebrospinal fluid clear, colourless, no cells; total proteid 0·1 per cent. Wassermann reaction negative in blood and cerebrospinal fluid.

DISCUSSION.

Mr. C. P. SYMONDS said that he had never seen a case of disseminated sclerosis in which the protein in the cerebrospinal fluid rose as high as 0·1 per cent.

(9) *Case of Syringomyelia.*

By Dr. S. A. KINNIER WILSON.

L. H., aged 16. Previous health: Diphtheria, "rheumatism" at the age of 4, and frequently since in legs, arms, and shoulders. Operation for adenoids when 10 years old. Twelve months' history of painless sores on the right hand and fingers.

November 12, 1922: Experienced a feeling of coldness in right half of body. At the same time she noticed that she could not appreciate the temperature of water with the right arm or hand. At the same period she noticed the left pupil was getting smaller and the left eyelid drooping.

On admission, December, 1922: Left pupil smaller than right, left eyelid drooping. Slight impairment of tactile sensibility, marked thermal and pain loss in left trigeminal area. Tongue on protrusion deviates slightly to the left. Very slight spasticity of right arm and leg. Right leg weaker than left. Sensory loss to pinprick and temperature over right half of body up to a transverse line in mid-cervical region. Faint diminution to tactile stimuli over the same area. Knee and anklejerks greater on right than on left side. Plantars: right doubtful, left flexor. Sphincters unaffected.

(10) *Case for Diagnosis, possibly Amyotonia Congenita.*

By Dr. S. A. KINNIER WILSON.

B. W., aged 11. Child born normally. Began to walk at normal age. He is the second youngest of eight children. At the age of 4 he was noticed

by his mother to be double-jointed. He began at this time to "fall about." The weakness of the legs has been progressive in the last three years. At present he is unable to stand unsupported.

Mentally the child is bright and intelligent. When sitting up the back is unduly rounded. The arms are thin and their strength poor. The muscular power of the legs is very poor. Impaired muscle tone in all limbs, the deficiency being greater in the legs than in the arms, over-extension at the knees on passive movements being very prominent. No contractures present. Arm-jerks very feeble. Abdominals active. Knee-jerks: Right greater than left, which is feeble. Ankle-jerks: Right feeble, left not obtained. Plantars: Right indefinite, left flexor. Sphincters unaffected.

(11, 12) *Congenital Neurosyphilis in Brother and Sister.*

By Dr. S. A. KINNIER WILSON.

(11) D. J., aged 10. Epileptiform fits since age of 5. Automatism, spitefulness. Mentally clear, Hutchinson's teeth. Pupils unequal, poor light reaction. Wassermann in blood, negative.

(12) G. J., aged 7. At the age of 5, paraplegia; unable to walk since arrest of mental development. Pupils Argyll-Robertson. Knee-jerks increased, plantars extensor, gait spastic and stamping. Ocular fundi, disseminated choroiditis. Wassermann in blood positive.

DISCUSSION.

Dr. JAMES TAYLOR said that in his experience two members of a family with congenital syphilis usually suffered in different ways. One of his patients, a boy who was afflicted with optic atrophy, was brought to hospital by a younger sister who had Hutchinsonian teeth, interstitial keratitis, and other signs of congenital syphilis, which were absent in the brother. The older patient eventually developed G.P.I. and died, whereas his sister remained free from symptoms of nervous disease.

The PRESIDENT said that Dr. Taylor's cases argued strongly against the assumption that there was a neurotoxic strain of the *Spirochæte pallida*.

(13) *Case of Syringomyelia, with much Sensory and Motor Impairment and little Wasting.*

By Dr. C. M. HINDS HOWELL.

M. G., aged 23. Patient "fell down" in a seizure or faint while at work in February, 1919. Afterwards she had an illness thought to be influenza. After the illness she was troubled with "hot sweats" affecting the left shoulder and left side of neck and head. Later she noticed weakness of the left hand while at work. In February, 1922, the right leg began to feel stiff and she had a sensation of cold waves passing up and down this limb.

On examination it is found that the left pupil is greater and the left palpe-

bral fissure smaller than on the right side. There is no nystagmus. There is partial loss of pain sense and of appreciation of cold over the left half of the forehead and over the lateral part of the left cheek. The left arm is weak, particularly the hand grasp; the thenar and hypothenar eminences are wasted. The deep reflexes are absent in the left arm. The right arm shows no weakness or wasting.

Both lower limbs are spastic, right more so than the left. The knee and ankle jerks are exaggerated and ankle clonus is present. Both plantar reflexes are extensor.

There is loss of tactile sensibility over the outer side of the right leg only. Pain sense is lost over both arms and both shoulders, and is impaired all down the right side of the trunk and over the whole of the right lower limb; on the left side of the body there is a similar impairment down to the lower border of the fourth dorsal segment both in front and behind.

Recognition of heat is completely lost over the whole of the right half of the body except the face, and over the left arm and left side of the trunk down to the level of the tenth dorsal segment. Loss of recognition of cold corresponds almost exactly in its distribution to the impairment of sensibility to pain.

(14) *Case for Diagnosis.*

By Dr. C. M. HINDS HOWELL.

G. S. In October, 1922, eight weeks before admission to hospital, patient's legs became weak while he was out walking; for about a week before that he had been losing the grip in the left hand and the left arm used to hang limply. Since the day when his legs gave way he has become steadily weaker and he has been aware of flickering in the muscles of his thighs. Since admission the right arm has become weak and he has become incontinent of urine and fæces. His neck has become stiff and it is painful when moved.

Examination: Left pupil slightly smaller than right. Fibrillation present in tongue. Complete flaccid palsy of left arm. Right arm becoming rapidly weaker. Abdominal and chest muscles weak; diaphragm does not seem to be acting. Left lower limb weaker than right. Fibrillation in muscles nearly all over the body, but especially in the thighs; wasting most pronounced in the muscles of the back and in the left lower limb. Sensory loss variable; fairly complete in both arms, less complete on chest with a level at the angle of the sternum. Sensory loss on the lower limbs much less than on the upper; right lower limb more affected than left. Reflexes: Knee-jerks brisk; plantars extensor.

Most of the signs presented by this case suggested the diagnosis of compression of the cervical region of the cord by a tumour. But this would not explain the fibrillation which was present. X-rays showed erosion of the second cervical vertebra and some shadows suggesting an intrathoracic tumour. As the condition was rapidly progressive he considered that it was

probably due to a diffuse sarcomatous or gliomatous invasion of the spinal cord. The cerebrospinal fluid contained 0·1 per cent. protein.

DISCUSSION.

The PRESIDENT described a somewhat similar case with total paralysis and anæsthesia of the right arm and partial paraplegia in which he had advised operation. The surgeon found no tumour, but noted no pulsations of the cord or dura mater. He therefore explored upwards under the laminal arches and came against a resistant mass. When he tried to break through this there was a gush of blood which proved, post mortem, to have come from an aneurysm of the posterior inferior cerebellar artery.

Dr. JAMES TAYLOR said that he had seen a similar case, which also presented the symptom of fibrillation of muscles, and which proved to be due to gliomatosis of the cord.

Dr. RIDDOCH described a case of quadriplegia with signs of spinal compression and multiple root lesions but with few sensory alterations, due to sarcomatosis of the meninges. The cerebrospinal fluid in this case was yellow, very highly albuminous and contained many tumour cells, some of which showed mitotic figures.

(15) *Case of Disseminated Sclerosis.*

By Dr. W. ALDREN TURNER.

G. W., aged 35. About one and a half years ago patient began to be troubled with a trembling of the right arm, becoming more marked when he used the arm; this tremor has gradually become coarser. About the time the tremor commenced patient's gait became somewhat unsteady. Fifteen months ago his speech became jerky and has got steadily worse up to the present. Four years ago patient fell off a bicycle, striking his head and bruising his right elbow.

Examination: Discs normal. Pupils unequal, left greater than right, regular, slightly eccentric, some retraction of eyelids, react normally. External ocular movements good, no nystagmus, squint or diplopia. Movements of face, palate and tongue normal. Numbness in both hands. No demonstrable loss to pinprick or cotton wool. Sense of position in space and localization of touch normal. No astereognosis. Violent intention tremor of the right arm, so great that it shakes the whole body. The tremor is not purely intentional, for it is sometimes present mildly in the shoulder during rest. The left arm shows a slight tremor of the intention type. There is no loss of power or limitation of movement. Arm-jerks: equal on the two sides; biceps-jerk not obtained. Right knee and ankle jerks greater than left. No ankle clonus. Abdominals: present and equal on the two sides. Plantars: both flexor. Gross ataxia of gait: the arms, especially the right, make large movements which react on the whole body. No Rombergism. Wassermann reaction negative. The cerebrospinal fluid is normal except that it gives a "paretic" curve with the Lange test.

Progress: Little change noticed in arms, though patient feels that the tremor of the right arm now involves the shoulder more. Both legs are affected by tremor and the left is now rather worse than the right.

Discussion.

Dr. Symonds said that he had noticed in the history of this case that the patient had had an illness called "influenza" six months before the onset of the tremor. He considered it possible that this was really a mild attack of encephalitis lethargica. He had seen involuntary movements follow an attack of encephalitis lethargica so mild as not to keep the patient in bed. He had observed Lange reactions of the "paretic" type in the cerebro-spinal fluid of two cases of encephalitis lethargica.

Dr. Riddoch was inclined to agree with Dr. Symonds in considering that this case was due to encephalitis lethargica. The steady onset of symptoms without any remission was unlike disseminated sclerosis. He had often noticed similar gross involuntary movements come on gradually after encephalitis lethargica.

(16) *Case of Unilateral Affection of the* 7, 9, 10, 11, *and* 12 *Cranial Nerves.*

By Dr. C. P. Symonds.

Miss T., aged 30. In July, 1919, she had some teeth extracted. Shortly afterwards she noticed a discharge from her left ear, for which she did not consult a doctor. This was followed by gradually increasing deafness in the left ear. In March, 1920, she first noticed hoarseness which prevented her singing. About the same time she began to experience pain in the left shoulder and found that this occurred especially when she attempted to carry heavy objects in the left hand. In the summer of 1921 her voice improved, so that she was again able to recite, though singing was still impossible. The pain in the left shoulder was also less noticeable. During the last year the voice has again become hoarser, and the trouble in carrying things with the left arm has increased. She has also occasionally noticed some difficulty in swallowing. In October, 1922, for the first time she had a brief attack of left facial spasm. In this the eye closed and the whole side of the face was screwed up. Since then she has had several such attacks.

On examination the positive findings are: Left-sided conduction deafness, together with a fleshy mass obscuring the membrana tympani, probably a polyp. A fragment has been removed for microscopical examination, which shows it to be a capillary angeioma. Left facial palsy of peripheral type. Paresis of the left vocal cord and left side of the palate. Weakness and wasting of the left sternomastoid and trapezius. Atrophic palsy of the left side of the tongue. Wassermann negative in blood. X-ray of head and upper cervical spine negative.

(17) *Case of Unilateral Affection of Cranial Nerves 9 to 12 (Tapia's Syndrome) associated with Chronic Otitis Media.*

By Dr. C. P. SYMONDS.

Miss C., aged 35. She has suffered from bilateral otorrhœa from time to time since childhood. She had tonsillitis at the age of 28, is subject to headaches, and has attended Guy's Hospital for constipation. In February, 1921, she first noticed hoarseness, and was referred from the medical to the throat department. It was there observed that the left vocal cord was paralysed. When seen a few days later the positive findings were: Paralysis of left vocal cord and weakness of left side of soft palate. Weakness and wasting of left sternomastoid and trapezius. Atrophic palsy of the left half of the tongue. Evidence of old-standing otitis media on both sides with a moderate degree of conduction deafness. The blood: Wassermann was negative. X-ray of the head and of the upper cervical spine showed no abnormality.

Under observation this patient has shown little change during the past two years except for the tendency of the hoarseness to diminish.

DISCUSSION (Cases 16 and 17).

The PRESIDENT considered Dr. Symonds's cases to be similar to those described in textbooks as "polyneuritis cranialis," the causation of which had been traced in some cases to otitis media.

Dr. COLLIER said that he had followed seven similar cases to autopsy, and in every case osteomyelitis of the base of the skull had been found. In one the disease had followed a bullet wound of the cranium; in another a tubercular osteomyelitis of the basi-sphenoid, and in the remainder ear disease was the cause. The appearance seen in the posterior fossa at autopsy was a plum-coloured cushion of raised and thickened dura mater with disintegration of the underlying bone. In every case the causative organism was a streptococcus. The long duration and the absence of pyrexia were remarkable. In one case there was no clinical evidence of otitis media, although the autopsy proved that this had existed. He placed no reliance on X-ray evidence in this condition, as it was very difficult to get satisfactory radiograms of the posterior cranial fossa. The cause of death in his cases had been lepto-meningitis in every case except the tubercular one, in which the carotid artery was eroded, and burst into the pharynx. One case had developed a hemiplegia, which was found to be due to thrombosis of the superficial veins of the brain. Replying to a question by Dr. SYMONDS whether the operative findings in Case 16 were not against his conception of the disease, Dr. COLLIER replied that in two cases following ear disease autopsy showed that the mastoid region was healthy, but that the infection had spread through the apex of the petrous bone.

Notices of Recent Publications.

Nerve Exhaustion. By Maurice Craig, C.B.E., M.D., F.R.C.P. Pp. 148. London: Churchill. 1922.

This small volume is intended as a guide to the treatment of nervous exhaustion, under which term the author includes a large number of morbid conditions, arising from many different causes; these are considered in detail. He treats very shortly of emotional shock, over-work, worry, and touches on physical states, such as puerperium and lactation, which lead to exhaustion. These various symptoms are attributed for the most part to "hypersensitivity," congenital or acquired, on which the author lays great stress. A chapter is devoted to sleeplessness, and the final section to treatment in general. The book is intended for the general practitioner, who is anxious to learn in simple language the means at his disposal for dealing with this aspect of the functional psychoneuroses.

Etudes Neurologiques. By Georges Guillain. Pp. 469. Paris: Masson et Cie. 1922. Price 25 francs.

The author has reprinted in this volume all those earlier papers in which he has brought forward any new facts related to the symptomatology and pathogenesis of nervous disorders. He has arranged them, not in chronological order, but in separate chapters according to the main subject with which they are concerned. The titles of these chapters reveal his wide interest and the valuable work he has done; the most important are: The fixation of poisons in the nervous system, pathology of the brain, pathology of the spinal cord, syphilis of the nervous system and tabes, muscular atrophies, changes in the cerebrospinal fluid, lethargic encephalitis and intoxications.

Many of the papers included are, it is true, only short communications originally published in various medical journals, and some perhaps are no longer of great interest or importance. But several of them at least have a real value, and the majority are certainly worth collecting together in a more permanent and easily accessible form. This is largely due to the fact that Guillain's interests have been mainly in the pathological and anatomical aspects of disease, and that his conclusions, as well as his hypotheses when he ventures on such, are solidly based on direct evidence of structural change. In fact in his introduction to this volume he insists that the anatomy and physiology of the nervous system must be the basis of any advance in knowledge which we can hope to attain, and that in the study of neuropathology all the modern methods of biology, bacteriology, chemistry and physics must be applied. A worker who has been guided by these principles must almost necessarily have valuable results to offer his readers.

Multiple Sclerosis (Disseminated Sclerosis): An Investigation by the Association for Research in Nervous and Mental Diseases. Pp. 241. New York: Hoeber, 1922.

The Second Annual Meeting of the American Association for Research in Nervous and Mental Diseases, which was held in New York in December, 1921, was devoted to a discussion on the etiology, pathology, symptomatology, differential diagnosis and treatment of disseminated sclerosis. The proceedings and conclusions of the commission are recorded in this volume, which constitutes a valuable contribution to our knowledge of this disease.

All the possible factors in the pathogenesis of the disease are discussed; several pages are even devoted to the hypothesis put forward by Jelliffe that as unconscious emotional factors are known to be under greater tension and more constantly operative than conscious ones which can produce somatic alterations, they may excite exudate phenomena in the blood-vessels of the nervous pathways intimately related to the function under repression, and therefore produce the characteristic lesions of disseminated sclerosis. But most of the papers and discussions are distinguished by a practical common sense. The sections on the vestibular and ocular manifestations of the disease are particularly interesting, and the negative results of Teague's prolonged research on its possible bacterial or protozoal origin are important in view of the recent repeated discoveries of causal micro-organisms. The chapters on the pathology of multiple sclerosis and on the changes that occur in the axis-cylinders are particularly complete.

The volume ends with a very comprehensive bibliography which, together with the statistical information collected in it, will prove extremely useful to all who wish to study the disease.

Der extrapyramidale Symptomenkomplex (das dystonische Syndrom) und seine Bedeutung in der Neurologie. By Professor G. STERTZ. S. 96. Berlin: S. Karger, 1921. Price 18 Marks.

This small monograph is devoted to those affections of the nervous system the most pronounced characteristics of which are disturbances in the functions of the motor system, and especially abnormalities of tone, unassociated with symptoms of affection of the cortico-spinal system. The clinical conditions included are progressive lenticular degeneration, pseudo-sclerosis, paralysis agitans, double athetosis, torsion spasm, spastic athetosis, choreic movements and myoclonia. In the second section the relations of the functional disturbances produced by non-systemic diseases of the basal ganglia, as arterio-sclerosis, disseminated sclerosis, tumour, encephalitis and poisons are considered; and the final chapter is devoted to a careful analysis of the pathology and physiology of the so-called extra-pyramidal systems. This is probably the section which will excite most interest, as subjects

claiming more and more importance in neurology are clearly and systematically dealt with in it. Unfortunately the author's style makes the reading of it difficult.

Beiträge zur Entwicklungsgeschichte des menschlichen Gehirns. Teil 2, Leiferung 1. *Die Entwicklung der Zirbeldrüse.* von Professor F. HOCHSTETTER. S. 45. Mit 6 Abbildungen im Text under 4 Tafeln. Wien und Leipzig: Deuticke, 1923. Price 10 Marks.

In this monograph, which is devoted to the development of the pineal gland in man and other mammals, Hochstetter has recommenced the issue of his valuable contributions to the embryology of the brain.

Certain features of disease of the pineal body have lately attracted considerable attention and consequently even to clinicians this monograph, in which many points on the origin and development of the gland are cleared up, offers some interest. It is, for instance, important that at one stage of growth the cells of its anterior lobe have an acinous or gland-like arrangement, suggesting a potential secretory function, which though not visible in the later stages of development may be reproduced in growths originating from these cells.

The plates by which the work is illustrated are extremely well reproduced, and make it possible to follow the descriptions of the text with ease.

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EDITOR.